Roche introduces

new Bactrim™ DS

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

double strength tablets

only 1 tablet b.i.d.
for better patient compliance

For chronic or frequently recurrent urinary tract infection.

Just 1 tablet b.i.d.

When the patient with chronic or frequently recurrent urinary tract infection fails to comply with therapy, persistent bacteriuria or relapse may occur. Single tablet b.i.d. dosage makes compliance easier.

Same efficacy with half the number of tablets

Studies have established bioequivalency of Bactrim DS double strength tablets with the Bactrim single strength tablets.

Greater economy for patients

Fewer tablets per day offer sufficient medication for the full course of therapy at a lower cost to the patient.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris* and *Proteus morganii.*

NOTE: The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register, 37*:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

Warnings: Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. **Data are insufficient to recommend use in infants and children under 12.**

Precautions: Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glositis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for children under 12. Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) every 24 hours
Below 15	Use not recommended

Supplied: Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole; fruit-licorice flavored—bottles of 16 oz (1 pint).

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double strength tablets
(160 mg trimethoprim and 800 mg sulfamethoxazole)

For chronic cystitis and pyelonephritis evidenced by persistent bacteriuria and due to susceptible organisms

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Med Trib 28

Medical Tribune

and Medical News

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Early Trials

M. Pneumonia Vaccine Seen Safe, Effective

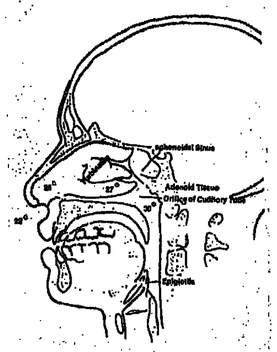
By Thomas Bulger
Medical Tribune World Service

MONTREAL—An experimental vaccine against Mycoplasmal pneumonia, the most common cause of pneumonia between the ages of five to 25, appears to be both safe and effective after initial trials in volunteers, the International Conference on Lung Diseases was told here.

The new vaccine, introduced intranasally rather than parenterally, consists of temperature-sensitive mutants of a virulent, wild strain of the organism, explained Dr. Michael B. Grizzard of the Laboratory of Infectious Diseases, National Institutes of Health.

The vaccine's effectiveness, he said, depends upon the natural temperature gradient of the human respiratory tract, which normally ranges from ambient air temperature at the nares to 37° C. in the lungs. The most promising strain in initial tests has been a mutant known as ts-H43, which replicates sufficiently freely in the temperatures of the upper respiratory tract to stimulate antibody production in local secretions, but will not replicate—and therefore will not itself cause pneumonia—at the core body temperature of 37°.

Continued on page 2



Intranasal mycoplasmal pneumonia vaccine under development at N.I.H. replicates freely at lower temperatures of upper respiratory tract, producing antibodies there, but is inactive at 37°C.

Beta Cell Auto-Antibodies Found In Insulin-Dependent Diabetics

By Frances Goodnight
Medical Tribune Staff

NEW YORK—The finding of antibodies reactive to pancreatic beta cells in the sera of certain diabetics offers fresh support for the hypothesis that autoimmune mechanisms are important in the etiology of insulin-dependent but not insulin-independent diabetes, according to investigators at the University of Maryland School of Medicine.

"We conclude that a state of autoaggression of pancreatic beta cells may underlie the pathogenesis of the majority of cases of insulin-requiring diabetes," Dr. Noel Maclaren said here in a report to the American Diabetes Association.

The study's results, Dr. Maclaren added, may be compatible with the concept that viral agents may initiate or precipitate insulin-dependent diabetes.

Tissue cultures of human insulinoma cells were used as model pancreatic beta cells since such cultures are free of other cell types, reproducible in long-term culture, and productive of "appreciable amounts" of immunoreactive insulin, the investigator explained.

Sera from 39 insulin-dependent diabetics, 15 insulin-independent diabetics, and 30 normal controls were examined for antibodies reactive to the cultured insulinoma cells. All sera were incubated with the insulinoma cells, and cell membrane antibodies were then identified with polyvalent goat-antihuman immunoglobulins by an indirect immunofluorescent technique.

Describing results, Dr. Maclaren said that 34 of the 39 insulin-dependent diabetics had positive antibody tests as judged by observation of more than 10 per cent positive immunofluorescent cells (a mean of about 23 per cent). The antibodies proved to be exclusively of the IgG and IgM subclasses.

One control serum and one insulin-independent diabetic serum showed positive results, with more than 10 per cent of cells immunofluorescent. The former came from a child with recurrent hypoglycemia and the latter from a 54-year-old man with alcoholism who had recently developed diabetes. The means of the control and insulin-independent diabetic groups were about 4 and 5 per cent, respectively.

Dr. Maclaren emphasized that the

Continued on page 13

Poll Finds 53% of MDs Favor Euthanasia for Trisomy 18

By Ben Rose
Medical Tribune World Service

TORONTO—A survey of physician attitudes to the management of severe congenital anomaly in the fetus and newborn in the San Francisco area shows that from 22 per cent to 53 per cent favor active or passive euthanasia, depending on the nature of the anomaly. The lowest figure was for Down's syndrome and the highest for Trisomy 18.

A total of 75 per cent favored development of diagnostic amniocentesis to enable screening of all pregnancies and 87 per cent favored parental choice of selective abortion of fetuses found abnormal.

A random selection of about one third of the obstetricians and pediatricians in the seven county Bay Area around San Francisco made up the survey group.

Continued on page 18

making rounds at press time

CANCER SURVIVAL - N.C.I. survey of 100 hospitals shows improved survival for prostate, testis, kidney, bladder, brain, thyroid, larynx, and skin melanoma cancer patients diagnosed during late '60s, compared with those diagnosed in '50s. Five-year breast ca survival rose from 60% in '50s to 64% in '60s. Survey covered whites diagnosed from 1960 to 1971.

MEASLES is rising in Midwest due to low immunization levels, according to H.E.W.-Chicago's Dr. E. Frank Ellis. He is also worried about low polio immunization. Midwest, he says, has the lowest such rate nationally; in 1974 only 58.3% of children 1-19 had had 3 or more vaccine doses.

Mechanism 'Grows With the Child'

Coiled Shunts Implanted in 3 Hydrocephalics

By Michael Herring
Medical Tribune Staff

WASHINGTON—A coiled ventriculoatrial shunt for hydrocephalic infants that "grows with the child" has been successfully implanted in three patients since 1972, surgeons at the Children's Hospital here have reported. The shunt, they said, could eliminate the present need for recurrent shunt-lengthening operations.

Drs. Thomas Milhorat, Chief of Neurosurgery, and James McClenathan, Chief of Thoracic Surgery, said sequential chest films "demonstrated the uncoiling of the atrial catheter in all cases."

A fourth patient, they said, died during operation from complications due to a severe brain defect. The other three had severe communicating hydrocephalus secondary to Haemophilus influenzae meningitis, with "extremely

Continued on page 18

Drawing diagrams the ventriculoatrial shunt, designed to uncoil with growth, that was successfully implanted in three infants by Drs. Thomas Milhorat and James McClenathan at the Children's Hospital, Washington, D.C. The doctors plan about 10 coiled shunt operations annually while continuing close observation of the original patients.

M. Pneumonia Vaccine Appears Effective

Continued from page 1

In the initial trial in human volunteers, fifteen individuals without evidence of M. pneumonia-related antibodies were infected intranasally by means of an atomizer, with 10^6-10^7 complement fixing units of ts-H43. During the 28 days of intense medical surveillance that followed, all volunteers showed evidence of infection, as indicated by shedding of the mutant or a positive serological response, but none developed signs or symptoms of illness, Dr. Grizzard said. Significant local antibody response could be detected in the nasal washings of 53 per cent, and in the sputum of 84 per cent (11/13) of those able to produce a sample.

Previous trials in hamsters have shown a positive antibody response to the mutant strain to be quite effective in stimulating long-term resistance to virulent M. pneumonia, lasting at least 18 months. The mutants have also proven to be genetically stable, with no tendency to revert to the wild type.

Data Compared

A larger, more recent volunteer study also shows a high rate of infection with the mutant, no febrile respiratory disease, but showed afebrile bronchitis in 7 per cent. Studies now in progress to determine the minimum effective dose of the vaccine indicate that volunteers receiving 10^4-10^5 CFU do not develop any signs or symptoms of illness; antibody response has not yet been determined.

The major burden of disease caused by M. pneumonia rests upon school-aged children and young adults, particularly those in closed populations, Dr. Grizzard noted. The organism causes pneumonia in military recruits with a frequency 25 times that seen in the general population.

Although antibiotics, notably tetracycline and erythromycin, are effective in reducing the clinical impact of these pneumonias, they are much less successful prophylactically, Dr. Grizzard explained. They are thought to merely delay rather than prevent the onset of overt disease. Prevention is an important goal for those individuals for whom a respiratory illness constitutes a special hazard, but the organism is a source of considerable morbidity in the general population as well.

The unusual form of administering the new vaccine, by intranasal innoculation, was tried after initial efforts showed that parenteral innoculation with inactivated organisms induced antibodies in the serum, but was not particularly effective in preventing infection or disease. This failure suggested that the wrong immune mechanisms were being stimulated, Dr. Grizzard said.

While systemic immunity does seem to be the prime mediator of resistance for those infections which undergo a systemic phase of dissemination, he said, it has been demonstrated in several respiratory diseases that resistance correlated directly with related antibodies in bronchial washings (IgA) but varied independently of serum antibody titers (IgG and IgM.)

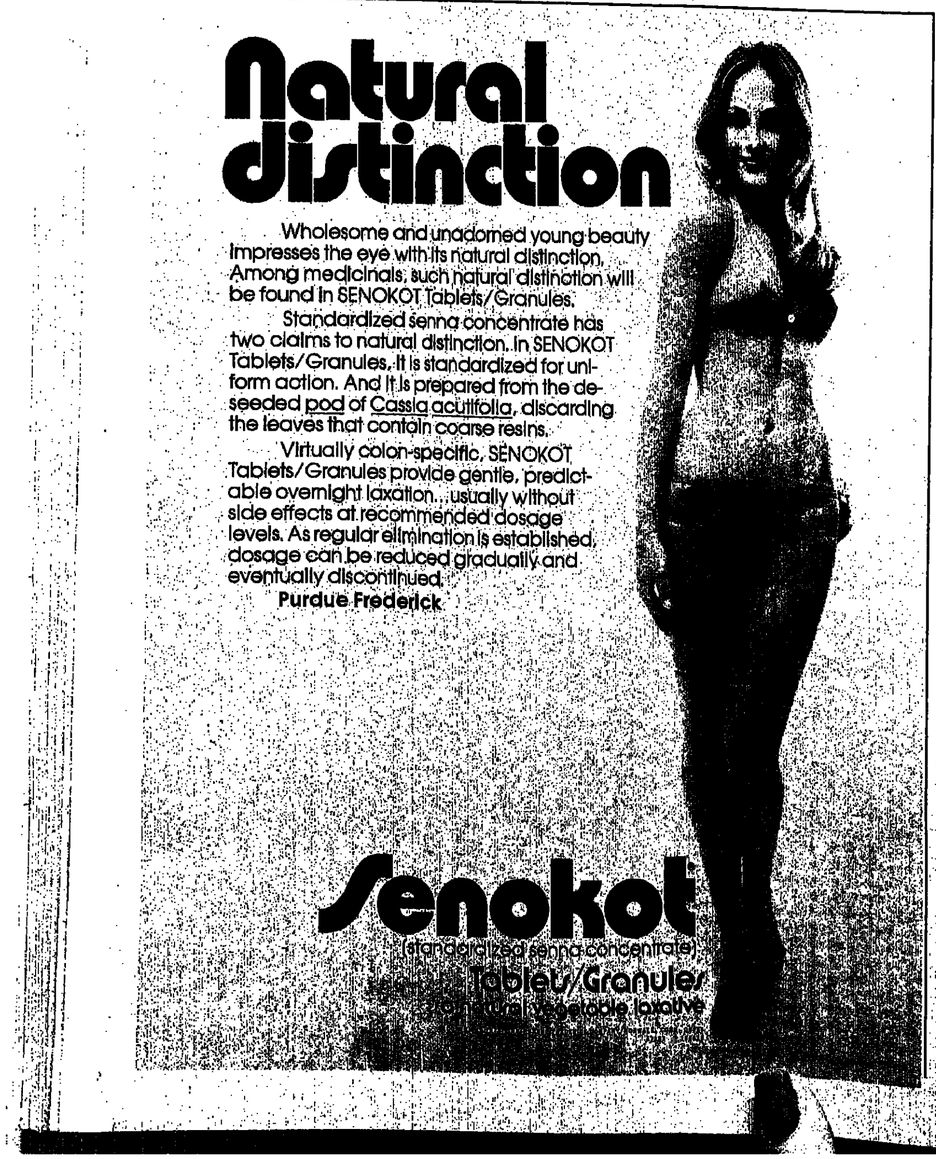
So far the evidence suggests that the M. pneumonia disease process is localized to the respiratory epithelium, so that local immunity would be expected to play a primary role. And, in volunteer studies, nasal IgA titers were the best predictor of who became ill and who remained well after challenge with a virulent strain.

Animal Tests Recalled

Previous tests in animals had also suggested the need for administering a live vaccine directly to the respiratory tract, Dr. Grizzard said. Parenteral administration of either live or inactivated organisms failed to prevent infection, disease, or subsequent lung pathology in hamsters later challenged intranasally. Nor was intranasal administration of inactivated vaccine sufficient: although it diminished the severity of the lesions, it did not limit the growth of the organisms in the lungs.

Finally it was demonstrated that either attenuated or virulent, live organisms, when administered locally, greatly suppressed infection and prevented pathologic pulmonary changes upon later challenge with virulent organisms. The advantage of the temperature-sensitive mutant of course, is that it does so without itself causing clinical disease.

Drs. Charles M. Helms and Robert M. Chanock were co-authors.



Relevance of Lab Studies On Tumor Cells Questioned

Medical Tribune Report

PHILADELPHIA—Since the tumor cells that scientists study in laboratories bear little resemblance to those that physicians treat in their patients, a great deal of research has not been clinically relevant, according to Dr. Michael Stoker of the Imperial Cancer Research Fund of England.

Speaking at the dedication of a new cancer research facility at Wistar Institute, he said that investigators, for example, must find closer models of naturally occurring cancer to contribute to better chemotherapy.

Dr. Stoker said that the isolated clones that he and other scientists have studied are necessary to get at basic mechanisms in cancer, but "the trouble arises and the criticism comes when we who work with these systems claim too much for them."

New Study Casts Doubt on Reserpine as Cause of Breast Cancer

Medical Tribune Report

LOS ANGELES—The hypothesis that reserpine—and other rauwolfia derivatives—cause breast cancer has been cast in new doubt by a California study showing that "when population controls were obtained from a uniformly wealthy population with a history of good access to medical care . . . measures of other drug use and of repeated consumption of medical care gave as high risk ratios as reserpine."

The results, reported in the *New England Journal of Medicine* (June 26) by Dr. Thomas M. Mack, Associate Professor of Community Medicine and Public Health at the University of Southern California, indicated that for the study population the "maximum likelihood estimate of the risk ratio for any use of reserpine was 1.2 and that for use at least five years before diagnosis [of breast cancer] was 1.6."

This risk ratio was described as "low," especially when compared with the 3.5 figure reported last fall in *Lancet* by the Boston Collaborative Drug Program. "Under the conditions of our study, if the true risk ratio were 3.5 as reported in Boston, the probability of finding by chance a risk ratio as low or lower than 1.2 would be less than 0.00001," Dr. Mack reported.

Recently, a Department of Health, Education, and Welfare short-term advisory committee reported hearing no new evidence confirming the three previous reports associating use of rauwolfia derivatives, including reserpine, with the development of breast cancer (MT, June 2).

'Main Problem' Cited

In an interview with MEDICAL TRIBUNE, Dr. Mack said that the "main problem" with the interlocking Boston, British, and Finnish studies reported concurrently in *Lancet* was that "they all used other patients as controls without taking into consideration the implications with respect to breast cancer." Each study compared the prevalence of drug use before diagnosis in cases of breast cancer for a general population to that of controls chosen from rosters of persons having other diseases.

Dr. Mack explained in his report that breast cancer is known to be associated with higher socioeconomic status, presumably by virtue of its association with late first pregnancy and perhaps other factors. Despite this fact, the controls chosen by the three study groups were of arguably lower socioeconomic status.

The Boston investigators choose controls from "urban hospital admissions, who tend to be not of higher but of lower income and education than the general population. Persons admitted for 'abdominal disorder,' 'respiratory diseases,' or 'trauma' to teaching hospitals in Boston seem likely to conform to this pattern," Dr. Mack suggested.

"The estimates of risk ratio from Britain and Finland," he continued, "were substantially lower than that in Boston, in accordance with more equitable care patterns, but are explicable on the same grounds. Finnish women with varicose veins and hemorrhoids are probably like their American equivalents in coming from families of lower income. . . .

"In the British study, other cancer patients served as controls. When patients with the low-frequency cancers found in Boston to consume an excess of reserpine were removed from the control group, the reservoir of reserpine use in the remainder was depleted. . . . Removal of those controls left a residuum consisting mostly of cancers tending to favor lower social classes. . . . We consider it possible that the recorded reserpine usage frequency in the British residual controls was an underestimate of that to be expected in the cases."

In contrast to these studies, Dr. Mack emphasized in his report, the California study investigated "cases of breast cancer from a community of uniformly high social class compared with controls chosen from the entire population of the same community."

The closed retirement community under study consisted of 17,000 nearly all white, relatively affluent residents, with a median age of 70, 85 per cent of whom used the community's comprehensive medical care facility as their major source of care. A four-year survey of this population ending in January 1975 revealed 120 new reports of breast cancer, Dr. Mack reported.

Nine cases were excluded, two having metastatic cancer and seven no charts at the medical center. For each of the 111 remaining cases, four controls were selected, most of whom were matched within six months on the bases of both age and entry into the community. The median age of the study group was 71.

Each of the charts was abstracted for first recorded drug uses through the date of diagnosis of cancer in the subject case in each matched set. The first recorded date of use of hypotensives, rauwolfia preparations such as *rauwolfia serpentina* and reserpine, thiazides, barbiturates, and estrogens (excluding contraceptive combinations) were noted. No attempt was made to establish current drug usage.

"As was to be expected in a population of this age and income level," Dr. Mack stated, "rates of drug use were very high. Over half the control women had used at least one of the drugs. . . . Over 90 per cent of the rauwolfia used was reserpine."

Further Analysis Described

Analysis revealed that for all medications abstracted "crude risk ratios were of the same order of magnitude" as reserpine use, Dr. Mack reported, "including those for measures of health consciousness: early clinic attendance and return of the entry questionnaire [completed at request of medical center upon entry into the community]. Use of barbiturates or of any of the drugs at least five years before diagnosis gave the highest crude risk ratios."

Dr. Mack also found that risk ratios for rauwolfia use in various subgroups of 99 matched sets (the 12 patients with a previous history of cancer being excluded) were of similarly low magnitude.

"All of these findings," Dr. Mack concluded, "are more consistent with an association between breast cancer and consumption of medical care than between breast cancer and reserpine. In fact, the question must be raised whether this association can be explained on the basis of known socioeconomic predictors of breast cancer."

Referring again to the previous study groups' method of comparing patients with breast cancer to other patients, Dr. Mack stated, "This approach may turn out to have been a common error because of the respective care patterns of persons at risk of breast cancer on the one hand and of serious illness on the other."

Dr. Mack elaborated on his conclusions for MEDICAL TRIBUNE: "Under the null hypothesis of no association, what would one expect to find comparing breast cancer patients to controls? Since breast cancer is associated with a slightly higher socioeconomic group, a random sampling of women would presumably reflect a slightly lower class than the breast cancer group. Now what do we expect in terms of reserpine use? Hypertension is a disease of the lower socioeconomic ranks so that if reserpine were randomly given to all people with hypertension, one would expect an inverse association [between breast cancer and risk of hypertension.]

Effect on Hypertension

"No inverse association has ever been noted," Dr. Mack continued. "For this and other reasons, people with the diagnosis of hypertension are probably of higher socioeconomic status than people with hypertension in general. We know from recent studies that hypertensives who receive care tend to have less severe disease and we also know that reserpine is given preferentially to mild hypertensives. Furthermore, borderline hypertensives tend as a group to be of higher socioeconomic class than people tested for hypertension in general. Finally, of the people who do get put on antihypertensive drugs, poor people tend to drop off.

"The net effect of this would be that people on reserpine at any given time might well also be of higher socioeconomic status, and if that's the case, then one might expect an association [of breast cancer patients and reserpine users] under the null hypothesis.

"Here I'm talking what would be expected if one picked people at random out of the population rather than choosing people with some other diagnosis. An even greater association would be expected if controls of lower than average socioeconomic rank were selected," Dr. Mack said.

Does the use of rauwolfia derivatives cause breast cancer? "I think the question is not settled," Dr. Mack told MEDICAL TRIBUNE. "I can't find any way to support the three previous studies, but this begs other evidence. As for the sometimes surprising association we found between breast cancer development and the consumption of medical services, other known risk factors, such as late pregnancy, could play a role, but perhaps they don't explain it entirely. It would be nice to know."

Dr. Mack declined comment on the advisability of giving rauwolfia derivatives on the grounds that he is not a hypertension expert.

index

CLINICAL NEWS NOTE: *"We concluded that a state of autoaggression of pancreatic beta cells may underlie the pathogenesis of the majority of cases of insulin-requiring diabetes." (Dr. Noel Mclaren of the University of Maryland at the American Diabetes Association, see page 1.)*

feature index

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reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

INDICATIONS
Hypertension. (See box warning.)

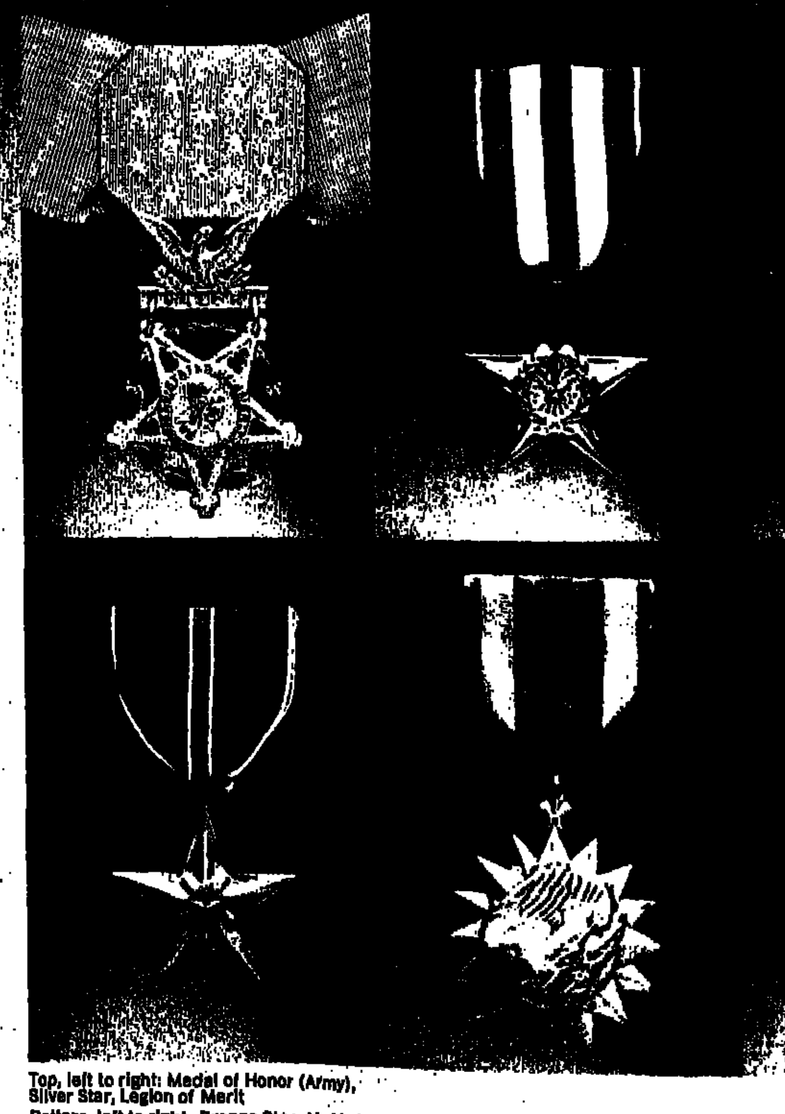
WARNING
This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

CONTRAINDICATIONS
Reserpine: Known hypersensitivity; mental depression (especially with suicidal tendencies); active peptic ulcer; ulcerative colitis; electroconvulsive therapy.
Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease.
Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

WARNINGS
Reserpine: Use with extreme caution in patients with a history of mental depression. Discontinue at first sign of despondency, early morning insomnia, loss of appetite, impotence, or self-deprecation. Drug-induced depression may persist for several months after drug withdrawal and may be severe enough to result in suicide.
MAO inhibitors should be avoided or used with extreme caution.
Hydralazine: Chronic administration of doses over 400 mg daily may produce an arthritis-like syndrome simulating acute systemic lupus erythematosus. This may also occur at *lower doses*. Long-term treatment with steroids may be necessary and residua have been detected many years later. CBC's, L. E. cell preparations, and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydralazine or if the patient develops any unexplained signs or symptoms.
Use MAO inhibitors with caution.
Hydrochlorothiazide: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.
Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.
Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.
Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma.
The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.
Usage in Pregnancy
Reserpine: The safety of reserpine for use during pregnancy or lactation has not been established; therefore, the drug should be used in pregnant patients or women of childbearing potential only when, in the judgment of the physician, it is essential to the welfare of the patient. Increased respiratory tract secretions, nasal congestion, cyanosis, and anorexia may occur in neonates and breast-fed infants of reserpine-treated mothers since reserpine crosses the placental barrier and appears in maternal breast milk.
Hydralazine: The drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.
Hydrochlorothiazide: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.
Nursing Mothers
Thiazides cross the placental barrier and appear in cord blood and breast milk.
PRECAUTIONS
Reserpine: Use cautiously in patients with history of peptic ulcer, ulcerative colitis, or gallstones (biliary colic may be precipitated).
Exercise caution when treating hypertensives with renal insufficiency. Use cautiously with digitalis and quinidine.
Intraoperative hypotension has occurred in hypertensive patients receiving rauwolfia preparations, but withdrawal of reserpine does not assure that circulatory instability will not occur in such patients.
Hydralazine: Use cautiously in suspected coronary artery or other cardiovascular disease, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced.
Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop.
Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported. If such abnormalities develop, discontinue therapy.

Salerno, Normandy, Iwo Jima, Inchon.

And still one more battle...



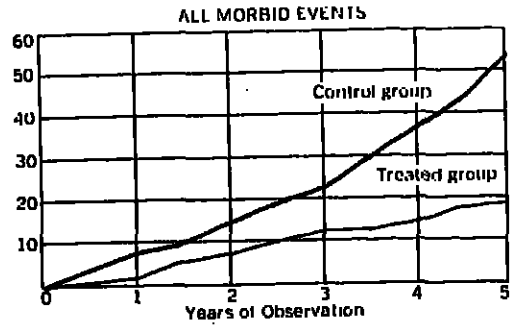
Top, left to right: Medal of Honor (Army), Silver Star, Legion of Merit
Bottom, left to right: Bronze Star, Air Medal, Purple Heart
Permission to reproduce medals granted by U.S. Department of Defense.

The battle against hypertension...

The VA studies demonstrated the need for therapy.[1,2]

In the VA study of 1967,[1] the patients were 143 male veterans with diastolic pressures averaging 115 through 129 mm Hg. In this group of patients with moderately severe elevations of pressure, antihypertensive therapy appeared to exert significant benefit.[1]

Further, in the study of 1970,[2] which examined effects of treatment in males with diastolic pressures averaging 90 through 114 mm Hg, it was found that even at these lower hypertensive ranges therapy exerted a beneficial effect.[2] The estimated risk of developing a morbid event over a 5-year period was reduced from 55% to 18%. Degree of benefit was related to prerandomization blood pressure levels.[2]



Estimated cumulative incidence of *all* morbid events over a five-year period as calculated by life-table method for patients with diastolic pressures averaging 90-114 mm Hg.

(Adapted[2])

Control was achieved[1,2] with...

hydrochlorothiazide

provides a mild antihypertensive effect through control of fluid volume; potentiates the activity of other antihypertensive agents.[3,4]

(a) Symbolized reduction in circulating fluid volume

plus reserpine

lowers blood pressure through sympathetic inhibition;[3,4] also produces a central sedative effect which may prove particularly useful in the management of the stress-reactive patient.

(b) Schema of norepinephrine depletion at sympathetic nerve ending

plus hydralazine

the unique action of hydralazine lowers blood pressure through direct arteriolar vasodilation to reduce peripheral resistance.[3,5]

(c) Diagram of relaxed arteriole

Only one antihypertensive agent contains all three components used in the two published VA cooperative studies.[1,2]

In the VA studies, Ser-Ap-Es was not used. However, all the components of Ser-Ap-Es were used in varying combinations and dosages.[1,2]

Ser-Ap-Es contains all the antihypertensive medication many patients will need.

And when the dosage of each component corresponds to the dosages preestablished by individualized titration, Ser-Ap-Es may prove more convenient and more economical.

The basic drugs used in the VA studies—hydrochlorothiazide, reserpine, and hydralazine—are original products of CIBA research.

Note: Use Ser-Ap-Es cautiously in patients with advanced renal damage or cerebrovascular accident. Discontinue at first sign of mental depression.

Ser-Ap-Es®
reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

Periodic blood counts are advised during prolonged therapy.
Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.
Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.
Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.
Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver diseases or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.
Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.
Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.
Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.
If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.
Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS
Reserpine: Gastrointestinal—hypersecretion; nausea; vomiting; anorexia; diarrhea. *Cardiovascular*—angina-like symptoms; arrhythmias (particularly when used concurrently with digitalis or quinidine); bradycardia. *Central Nervous System*—drowsiness; depression; nervousness; paradoxical anxiety; nightmares; rare parkinsonian syndrome and other extrapyramidal tract symptoms; CNS sensitization (manifested by dull sensorium, deafness, glaucoma, uveitis, and optic atrophy). *Miscellaneous*—frequently nasal congestion; pruritus; rash; dryness of mouth; dizziness; headache; dyspnea; syncope; epistaxis; purpura and other *hematological reactions*; impotence or decreased libido; dysuria; muscular aches; conjunctival injection; weight gain; breast engorgement; pseudolactation; gynecomastia; rarely water retention with edema in hypertensive patients.
Hydralazine: Common—headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent*—nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura; hypotension; paradoxical pressor response.
Hydrochlorothiazide: Gastrointestinal—*anorexia, gastric irritation,* nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo, paresthesias, headache, xanthopsia. *Dermatologic-Hypersensitivity*—purpura, photosensitivity, rash, urticaria, necrotizing angiitis, Stevens-Johnson syndrome, and other hypersensitivity reactions. *Hematologic*—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. *Cardiovascular*—orthostatic hypotension may occur and may be potentiated by *alcohol, barbiturates, or narcotics*. *Other*—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSAGE
As determined by individual titration (see box warning).
Usual dosage is 1 or 2 tablets t.i.d. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by *at least 50 percent*.

HOW SUPPLIED
Tablets (dark salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 15 mg hydrochlorothiazide; bottles of 30, 60, 100 and 1000.
Consult complete literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

3/4911 17

CIBA

Editorial Capsules

. . . brief summaries of editorials or comments in current medical and scientific journals.

Suicide in Children

"The myth that children do not become clinically depressed, only miserable, has been firmly squashed by a number of recent observations. The misconception has survived until now because depression in children and young people is often expressed in indirect ways—feelings of boredom, being fed-up, finding nothing worthwhile to do, believing their appearance, their selves, and the world to be all wrong—or it is cloaked by aches and pains, dangerous excitement-seeking, or delinquency.

"Children and young people do not only threaten suicide; they may carry out their threats . . . [A careful study in England and Wales of suicide in children under 14 years revealed that] 31 children and young people killed themselves. . . .

"No child under the age of 12 years killed himself. More boys than girls committed suicide . . . Suicide notes indicated intense feelings of anger and a wish to avoid punishment or humiliation for disciplinary problems at school.

"The age of onset at 12 years coincides with pubertal changes with their associated adolescent turmoil, a maturing concept of death, and less supervision giving more opportunity to carry out suicidal acts. What factors should alert the practitioner to think about the possibility of suicide? Should threats of suicide be taken seriously? Only 40% of the child suicides had in fact made threats beforehand, while up to 10% of referrals to child guidance clinics in one series had made suicidal threats or gestures.

"Suicidal threats should, then, be taken seriously as cries for help. . . .

"Personality profiles found commonly among suicides included solitary children of superior intelligence attending grammar schools, culturally distant from less well-educated parents; often the mothers were mentally ill and the children depressed, in conflict and withdrawn, having stolen or stayed away from school. Another group were impetuous, aggressive, with violent outbursts, suspicious and resentful of criticism and again often in trouble at school. These are familiar clinical patterns and there are additional factors which may give suggestive pointers—disturbed family backgrounds and divorce, and families where parents or siblings provide models by having attempted or succeeded in committing suicide. Access to means and the opportunity are the final factors, and this can include literature describing ways of committing suicide.

"These children have met 'failure' of emotional support in their environment early in their lives, and as Winnicott stated 'it is the death that happened, but was not experienced, that is sought . . . sending the body to death, which has already happened in the psyche . . . suicide is no answer . . . it is a despair gesture.'" *(Editorial, Brit. M. J. 1:592, Mar. 15, 1975)*

Ischemic Legs Salvaged in Diabetics By Femoral-Popliteal Artery Bypass

Medical Tribune Staff

NEW YORK—"Significant salvage of severely ischemic limbs can be achieved in diabetic patients in lieu of primary amputation," Dr. Frederick A. Reichle told the 35th annual meeting of the American Diabetes Association here.

Femoral bypasses to the popliteal or tibial arteries in 168 diabetics proved comparable to or only slightly less successful than similar operations in nondiabetics, he said, adding that "the function of the bypasses is also good over a long period of time."

Dr. Reichle, who is Associate Professor of Surgery and chief of peripheral vascular surgery at Temple University's Health Sciences Center, said, "the operation is done mainly for patients that otherwise would not be able to keep their leg. We wish that salvage was 90 or 100 per cent, but we still feel that even 60 to 80 per cent is better than primary amputation.

Preoperative angiograms were used to determine the extent of arterial damage, Dr. Reichle said, and the need for bypass surgery was determined chiefly by a diagnosis of rest pain, ischemic ulceration, or gangrene. In addition, cellulitis, obstruction of major arteries, infection, and claudication were sometimes present.

A total of 364 patients, of whom 46 per cent were diabetic, underwent lower-limb salvage operations. Ninety-two diabetics and 132 nondiabetics received femoropopliteal bypass, and 76 diabetics and 64 nondiabetics femorotibial bypass.

Initial limb salvage after femoropopliteal bypass was achieved in 82 per cent of diabetics, compared with 80 per cent of nondiabetics, Dr. Reichle reported. With femorotibial bypass, the success rate was 60 per cent for diabetics and 78 per cent for nondiabetics.

Six weeks postoperatively, six of the 168 diabetics (3.6 per cent) were dead, and four of the 196 nondiabetics (2 per cent).

One-to-11-year follow-up of surviving patients in whom initial limb salvage was achieved showed delayed graft occlusion to be lower in the diabetics than the nondiabetics.

Coinvestigators were Drs. Charles R. Shuman and R. Robert Tyson.

The familiar refrain of depression: morning fatigue... sadness... anorexia... insomnia

Now, Merrell offers Norpramin (desipramine hydrochloride tablets N.F.) to effectively relieve these common manifestations of depression.

Norpramin also provides additional benefits in treatment of your patients.

☐ effectively relieves physical, psychological and emotional symptoms of depression

☐ minimal daytime sedation—important for patients who must be alert to perform daytime activities

☐ relief that may begin in 2 to 5 days—but full therapeutic effect is seldom seen before 2 weeks

☐ side effects rarely require discontinuation of therapy

Prescribe Norpramin to change the familiar refrain of depression in your practice.

Norpramin® (desipramine hydrochloride tablets N.F.)

Brief Summary

MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215

Norpramin (desipramine hydrochloride) lightens and brightens the days of your depressed patients

Merrell

FDA Label, Ad Warnings Dissatisfy Critics of Clindamycin, Lincomycin

Medical Tribune Report

WASHINGTON—Although the F.D.A. is changing its advertising regulations to warn doctors of the sometimes fatal consequences of prescribing clindamycin and lincomycin, Senator Gaylord Nelson (D.—Wis.) believes that "the harm has already been done with respect to these drugs."

Dr. Sidney Wolfe, director of Ralph Nader's Health Research Group, also told MEDICAL TRIBUNE that the agency's warning "isn't strong enough," while an Upjohn spokesman contended, "It's really a matter of semantics."

Dr. Pete Rheinstein, director of the division of drug advertising for the Bureau of Drugs, explained that the new regulations will require that in any statement of a drug's indications and limitations, "equal prominence must be given to the words of limitation."

In the case of the two antibiotics, the Upjohn company complied in March with new text for indications, stating that the drugs "should be reserved for penicillin-allergic patients or other patients for whom, in the judgment of the physician, penicillin is inappropriate."

There is also a warning box, prominently displayed in advertising and on labels, stating that both lincomycin and clindamycin "can cause severe colitis that may end fatally." An Upjohn spokesman added that the number of adverse reactions "is not of the magnitude cited in the hearings; nevertheless, we have gone along with the warning."

However, Dr. Wolfe insisted that the indications should have limited the drugs to "both penicillin-allergic *and* erythromycin-allergic patients—something the F.D.A. did not require the company to put in their new advertising and package."

Dr. Wolfe also said he had recommended to the F.D.A. that the drugs be limited to hospital patients and to those who were started on either drug sider the proposal, he said.

"There are still a lot of people who might be put on these drugs when they should be put on erythromycin, which is infinitely less toxic," he explained. The number of people allergic to both penicillin and erythromycin is "infinitesimally small," he noted.

Senator Nelson, who is chairman of the Senate Monopoly Subcommittee of the Select Committee on Small Business, stated recently that testimony earlier this year "revealed that more than 7,000,000 patients per year have been exposed needlessly to the dangers of serious side effects from using clindamycin and lincomycin, when safer and more effective drugs are available."

According to the F.D.A.'s own evidence, he said, 95 per cent of the people taking them should never have been given these drugs.

The harm has already been done, he added, because both antibiotics have been "vigorously advertised and promoted for years. Testimony by marketing experts holds that when a product is heavily advertised over a long period of time, there may be a deep and long-lasting impact on the attitudes, beliefs, and behavior of consumers—or, as in the case of drugs, prescribers," he said.

"In other words, . . . some messages for some products under certain conditions are extremely difficult to eradicate," he explained. "This has been demonstrated with drugs such as chloramphenicol, panalba, as well as other antibiotic combinations that became the most widely used drugs on the market, although medical experts continually issued warnings about their dangers."

45 Deaths Reported

The dangers from clindamycin and lincomycin are now well-known: so far, some 45 deaths from bloody colitis have been reported.

"These are only reported deaths," Dr. Wolfe told MEDICAL TRIBUNE. He suggested that there is often a 10-fold error in reported figures because the reporting systems are voluntary and "fraught with the thought in the minds of doctors that they are setting themselves up for a malpractice suit by reporting."

There may thus be hundreds of deaths from colitis, he said, and "thousands upon thousands of less severe cases, if the figure of the one prospective study is correct."

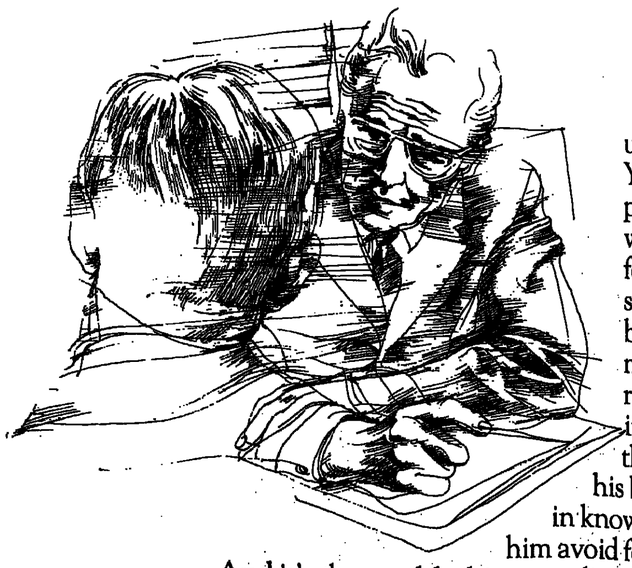
Dr. Wolfe made reference to a Washington University study reported last October in the *New England Journal of Medicine*, in which hospitalized patients were given clindamycin and examined periodically by sigmoidoscopy for signs of colitis. The researchers found that 10 per cent of patients developed colitis as a side effect, he said.

"The colitis was mild in some people," Dr. Wolfe told MEDICAL TRIBUNE, "but the point is, this is not some rare adverse drug reaction. It's happening very commonly.

"Clindamycin is a good antibiotic for treating anaerobic infections," he added, "but these are almost always serious enough to merit hospitalization and, according to the survey data on hospital infections, occur only some 2 or 3,000 times a year."

"Let me tell you about the medicine I'm going to prescribe."

TALKING OVER VALIUM®(diazepam) THERAPY WITH YOUR ANXIOUS PATIENT.



A patient often benefits by a greater understanding of his treatment program. You may find it helpful to make your patient aware that the purpose of therapy with Valium is to help reduce discomforting and disabling symptoms of excessive psychic tension and anxiety. It is beneficial for him to understand that much of his tension and anxiety can be relieved by your reassurance and counseling, and that these measures can do more than anything else to help him cope with his basic problems. The patient is reassured in knowing he can expect his medication to help him avoid feeling overwhelmed by his symptoms. And it's also good for him to realize that he will be taking Valium only as long as he needs it.

Your expressed confidence in the medication prescribed, and the positive atmosphere in which therapy is given and accepted, work to the patient's advantage.

"It's important that you follow my directions closely."

Selection of a dosage regimen is an important consideration when Valium (diazepam) is prescribed, and dosage should be individualized to achieve maximum beneficial effect. If the patient understands clearly when and how much to take, and if he knows why it's to his benefit to follow the regimen closely, the chances are better that he will take the medication precisely as directed. That should help avoid missed doses and discourage taking too much or too little medication—all of which can have an undesirable effect on the management of the patient's condition.

"I'll see you again the week after next and we'll see how you're making out."

Your patient is often likely to feel reassured when you talk about seeing him again to check his progress. A planned visit evidences your continued interest and affords the patient an opportunity to report improvement he has made and to relate whatever continuing or additional difficulties he may be experiencing. It's also a chance for him to describe his response to therapy with Valium.

During follow-up visits, as your patient talks about his medication and about its effects on his symptoms, he will provide the kind of information that will be of great help in evaluating total therapy, adjusting the dosage of Valium, or discontinuing the medication entirely if that seems indicated.

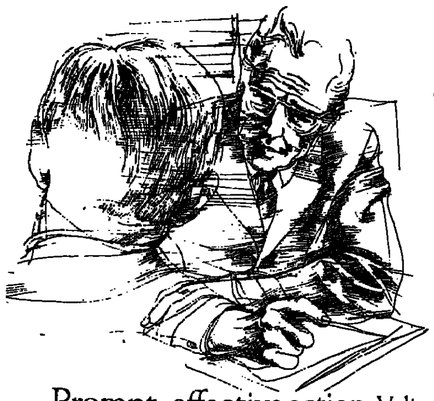
Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets

for individualized treatment of psychic tension

ROCHE

Please see the following page for a summary of product information.



Valium® (diazepam)

2-mg, 5-mg, 10-mg scored tablets

Prompt, effective action. Valium (diazepam) works rapidly to relieve pronounced psychic tension in patients overreacting to stress and in psychoneurotic patients.

Wide margin of safety. Valium is generally well tolerated and in usual dosages rarely produces significant adverse reactions. (See prescribing information below.)

Dosage flexibility. Scored Valium 2-, 5-, and 10-mg tablets give you dosage flexibility no tranquilizer capsule can match.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.

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The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune

and Medical News
Published by Medical Tribune, Inc.

"Science Must be Without Deceit—Must be Impeccable."

"*Science must be without deceit—must be impeccable.*" This statement by Alexander M. Schmidt, M.D., FDA Commissioner, must be the bedrock not only for drug regulatory activities but for biomedical research in general. This standard must be applied with absolute rigor to drug companies and to the FDA as well.

It is precisely because this standard has not been met that MEDICAL TRIBUNE has taken strong exception to some of the actions of the FDA and of certain drug companies. In respect to the FDA, the dictum that Caesar's wife must be above suspicion applies, that the standards it sets be of the highest quality, "beyond reproach" in terms of its work, that it be "impeccable" in its objectivity and its decision-making, and that it be free of the "deceit" which is implicit in double standards or "expediency" testimony at legislative hearings, which have more to do with politics than with the problems of care for the sick and the prevention of disease.

It is high time that it be recognized on all sides, political as well as scientific, social as well as industrial, that the interests that must rule are not those of a bureaucracy, not those of individuals with political aspirations, not those of activists with consumerist ambitions, not those of the drug companies, not even those of physicians generally—but the interests of those to whom we are ultimately responsible, who are the raison d'etre for medicine and the related professions—our patients, who are all the people of the United States and the peoples of other nations as well.

A.M.S.

Algorithm Anyone?

MEDICAL LANGUAGE, like any living language, is subject to change and even mutation, which may be entertaining or irritating, depending on one's humors and crotchets. Some nine years or so ago we inveighed against the sudden introduction of "nosocomial infections" in the literature, noting that of 40 people checked only one, who had studied Greek, knew that a *nosocomion* was a hospital. Currently, we hope, everyone knows.

Four years prior to the sour comments on the advent of nosocomial, we complained about the sudden appearance of "parameters" in medical writing. We noted that parameter had a very precise meaning for mathematicians and physicists and, after defining it, lamented that "suddenly we find blood counts, blood pressures, serum cholesterols, weights, heights, ages, sex —in short anything having to do with a patient—happily described in medical literature as parameters." By now, the latest editions of medical dictionaries include parameter in their lexicons. *Stedman's* 22nd Edition, haughtily and with more or less accuracy, defines it as, "An arbitrary constant in a mathematical expression, which can possess different values, each value defining another family of equations. In $y=a+bx$, a and b are parameters. A quantity that describes a population (not the estimates or values of that quantity)."

But *Dorland's* 25th Edition copes with current usage, adding a sort of devious and untrustworthy rationalization: "a variable whose measure is indicative of a quantity or function that cannot itself be precisely determined by direct methods; e.g. blood pressure and pulse rate are parameters of cardiovascular function, and the level of glucose in blood and urine is a parameter of carbohydrate metabolism." Oh well, that's how language mutates.

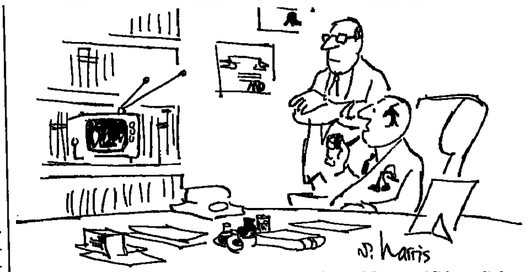
Yet all this is by the way, for the pathogenesis of this editorial is the popularization of a relatively new word in medical writing, namely *algorithm*. It has not yet been admitted into the medical dictionaries but give them time, give them time. Algorithm is a variant of algorism (after a Persian mathematician) and, as defined in the indefatigable *Webster's* Third New International Dictionary, is the art of calculating by means of Arabic numerals, i.e., 0, 1 . . . 9. *Van Nostrand's Scientific Encyclopedia* adds that algorithm is now used for any method of computation, algebraic or numerical, or any method of computation using a comparatively small number of steps.

A more recent dennition by a mathematician states that algorithm is a list of instructions for solving a problem.

Well, then, how is algorithm being used in the medical literature? Apparently when a subject, e.g., a disease, is presented in a more or less simplified form, or a synopsis, using a comparatively small number of steps, those doing so have taken to describing it, heaven help us, as an algorithm.

A Shunt to Grow With

CLINICAL QUOTE: *"These results are encouraging and suggest that when a ventriculocardiac shunt designed for adults is coiled in a Silastic pouch and implanted in the chest of an infant, the atrial catheter will elongate with growth. Needless to say, we make no claims concerning the long-term benefits of direct cardiac shunting. We anticipate that complications will arise as they do with all shunting procedures, and it remains to be seen how difficult the management of such problems will be."* (Drs. Thomas Milhorat and James McClenathan, Children's Hospital, Washington, D.C., see page 1.)



"Interesting game. In the first inning one of the Red Sox was hit by a pitch, and another was spiked. Then, one of the Yankees wrenched his shoulder, another's trick knee gave out..." © 1975, Medical Tribune, Inc.

LETTERS TO TRIBUNE

When Life Begins . . .

Although I did not have the opportunity to read the letter by Dr. John Henry Rowland, Jr. (MEDICAL TRIBUNE, May 7), I was interested in reading the three rather sarcastic responses to his letter, printed in MEDICAL TRIBUNE of June 4. I would simply like to respond to the first two letters by Paul Singer, M.D., and G.W.F. Schroeder, M.D. Their point seems to be that human life is a continuum, including viable sperm and unfertilized viable ova. The third letter by Dr. Walter H. Szchoff then equates the fertilized ovum or viable fetus with carcinomas.

The question in abortion is not, "Is abortion the destruction of living human tissue?" but the question is, or should be, "Is abortion the destruction of a new unique individual human being?" Contrasted to viable sperm or viable ova or a benign or malignant tumor, the unborn fetus is genetically completely unique. The unborn fetus constitutes a unique combination of genetic material completely distinct from the genetic composition of its mother, in whom it now resides, or from its father, who contributed to its development. Therefore, your three respondents to Dr. Rowland's letter have begged the question of whether abortion is the destruction of a unique individual human life.

As we consider the question of whether abortion is something physicians should now in the 20th century begin to endorse (reversing a track record of condemning abortion for the past 2400 years, since the time of Hippocrates, the father of medicine), let us avoid as much as possible sarcastic blurring of the facts of embryology and genetics.

KARL H. BRENNER, M.D.
Roswell, N.M.

BOOK BIOPSY

This new MEDICAL TRIBUNE *feature is not a book review, but an attempt to extract from the book itself a few quotations to show its character and possible usefulness.*

ACUPUNCTURE AND MOXIBUSTION—*A Handbook for the Barefoot Doctors of China. Translated by Martin Elliot Silverstein, I-Lok Chang, and Nathaniel Macon; Schocken Books, New York; $7.00; $2.95 paperback.*

From the translators: "We emphasize that we are not, and never have been, experts on or practitioners of acupuncture, moxibustion, or any of the Chinese medical arts. We do not know whether these procedures are, indeed, valid therapeutic techniques. We have not been in contact with the authors or publishers of the original Chinese work, feeling that this separation helped to preserve the freshness of our viewpoint and the integrity of our translation. The translation is not authorized by either the Chinese or the United States government.

"We present this translation . . . without advocacy, evaluation, or recommendation. . . .

From the authors: "The text is divided into two major parts. The first part introduces basic aspects of the techniques and several basic methods of actual physical application, along with a discussion on ninety-two commonly used anatomical acupuncture points. The second part deals with the therapy for certain common illnesses, . . . occurring in farming communities . . . with an evaluation of its effectiveness. The fewest number of body points necessary for the treatment are indicated. Practicability is stressed so that a beginner can master the subject . . .

"The preparation of a text is a new experiment to us. In order to be certain that the text will accommodate the actual need of the farming community, we have given the first draft to the students in medical workers' training classes, organized discussion groups afterward, and requested the comment of the instructors. We have made several revisions, and finally arrived at the present text . . .

". . . We sincerely hope that the instructors and the readers, through their practical use of the text, will communicate to us suggestions for future editions.

". . . we are preparing a text entitled *The Essentials of Chinese Medical Methods*. Together with the present text, the two texts may be used for a one-year training course on an apprentice basis."

The Department of Health,
Ho Pei Province

Microsurgical decompression of cranial nerve root entry-exit zone is achieved as superior cerebellar artery (a) is raised by dissecting probe (d) to relieve impingement on the trigeminal nerve (T). Other letters indicate pons (p) at upper right, retractor blade (r) lower right, and vein (v) behind probe.

Tic Douloureux Is Eliminated By Nerve Root Decompression

Medical Tribune Report

NEW YORK—Definitive treatment of trigeminal neuralgia and hemifacial spasm can be achieved by microsurgical decompression of the nerve root entry-exit zone, the American Neurological Association was told here.

Dr. Peter J. Jannetta, of Presbyterian-University Hospital, Pittsburgh, said that observations made in more than 280 such procedures indicate that both syndromes appear to have a "simple and precise mechanical cause"—cross-compression of this zone, usually by arterial loops.

Vascular decompression with placement of a small plastic prosthesis to prevent re-impingement on the nerve has proved to be safe and effective therapy, he reported, and precludes resort to nerve destruction.

Unsuspected Tumors Found

Results obtained with the treatment in the first series of 60 patients having classic intractable trigeminal neuralgia (TG) and 45 having hemifacial spasm (HFS) were described by Dr. Jannetta.

Tumors that had been unsuspected preoperatively were found and removed in five of the TG patients and in one HFS patient. A sixth TG patient had multiple sclerosis and the presence of a plaque at the root-entry zone of the nerve required nerve section.

The remaining patients experienced gradual improvement in symptoms and nerve function following decompression, Dr. Jannetta said. Criteria for success included facial sensory testing and electromyography done before and after decompression.

Four TG patients did have sudden recurrence of symptoms a few days after treatment, he noted, but at reoperation it was found that slippage of the prosthesis had allowed the artery to press again on the nerve. Insertion of another prosthesis was effective, and there have been no late recurrences.

Mild sensory abnormalities seen preoperatively in TG patients who had not undergone any prior surgery cleared soon after decompression, according to Dr. Jannetta. However, facial numbness caused by "prior destructive procedures" for trigeminal neuralgia diminished slowly and did not completely

After microsurgical decompression of nerve root entry-exit zone is performed, surgeon obtains vascular decompression with placement of small plastic prosthesis (s) to prevent re-impingement of artery (a) on trigeminal nerve.

Medical Tribune
sexual medicine today
the physician's ...

don't miss the next
sexual medicine today

the male reproductive system—Last month we reported on new developments in female fertility control, as reported at the eighth World Congress on Fertility and Sterility, in Buenos Aires. Part II will deal with male reproduction—with specific focus on sperm banks, therapeutic fertility agents, steroidal contraception and male "menopause"....

diagnosis: impotence—New York psychiatrist Dr. Morton Golden tells why the impotent patient often camouflages by "escaping into a vague, somatic complaint".... why physicians may be hampered in treatment by fears over their own waning sexual powers.... why "psychological support is the key" to symptom reversal....

patients' quandaries about nudity—the second of two articles that candidly probes changing physician attitudes toward nudity.... presents questions some patients are asking—about nudity in sexual intercourse, at the beach, in group therapy, to name some—and thoughtful answers given by doctors and by authorities in related disciplines....

Antibodies Are Linked to Juvenile Diabetes

Continued from page 1

presence of antibodies seemed unrelated to insulin therapy. The test was positive in eight sera obtained at the onset of insulin-dependent diabetes, the majority of the negative tests in this type of diabetes were seen in patients with disease of long duration, and the addition of porcine insulin to positive sera before antibody testing in a separate experiment did not influence results.

The investigators next explored the possibility that insulin-dependent diabetics harbor sensitized lymphocytes that will react with insulinoma cells, Dr. Maclaren said.

"When lymphocytes from insulin-dependent diabetic children were incubated together with insulinoma cells over a three-day culture period, it was apparent that the lymphocytes became strikingly adherent to these insulin-secreting cells," he commented.

It also became apparent, the investigator said, that accelerated insulinoma cell death occurred in the presence of diabetic lymphocytes. By contrast, lymphocytes from control subjects did not manifest cytoadherence.

Since both antibodies and sensitized lymphocytes reactive to the model beta cells were observed in the circulation of insulin-dependent diabetics, efforts were then made to determine their relative roles—if any—on insulinoma cytotoxicity.

Dr. Maclaren cited three mechanisms by which possible autoimmune beta cell cytotoxicity might be mediated: by specific antibodies to beta cells in conjunction with complement; by antibody-independent lymphocytotoxicity, a function associated with thymus-derived ("T") lymphocytes; and by antibody-dependent lymphocytotoxicity, produced by what are operationally defined as bone marrow-derived ("B") lymphocytes.

Test Results Compared

To test these possible mechanisms, sera and/or lymphocytes from 23 insulin-dependent diabetics and 12 control subjects were incubated with insulinoma cells and studied at the 40-hour stage.

The results demonstrated no significant insulinoma cell death in the presence of diabetic as compared to control sera, Dr. Maclaren said. However, diabetic lymphocytes showed "a striking and significant insulinoma cytotoxicity in comparison to control lymphocytes." And the addition of diabetic serum to diabetic lymphocytes also resulted in a significant insulinoma cytotoxicity compared to that of control serum-plus-lymphocytes.

Further tests in which diabetic T and B lymphocyte subpopulations were isolated and studied for cytotoxicity of insulinoma cells indicated that both antibody-dependent (B lymphocyte) and antibody-independent (T lymphocyte) cytotoxicity were operative.

Coauthors of the report were Drs. Shih-Wen Huang, Bruce P. Hamilton, and Marvin Cornblath, and Glen E. Taylor.

Endoscopy Directs Drugs into Bile Duct

Medical Tribune Report

SAN ANTONIO, TEXAS—Realization of a key step in the development of a nonoperative treatment for gallstones located inside the bladder was reported at a meeting of the American Society for Gastrointestinal Endoscopy during Digestive Disease Week.

It has now been found to be possible to introduce drugs under direct visualization into the common bile duct and gallbladder for dissolving stones by a new endoscopic approach devised by Dr. Keiichi Kawai, Professor, Department of Preventive Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan.

While he was able to apply the procedure itself successfully in five patients, Dr. Kawai explained that since existing substances that dissolve gallstones are too toxic when injected into the bile, he used a different one that did not give satisfactory results. Biochemists associated with his team are working on the problem of producing an adequate solvent.

Dr. Kawai also reported new follow-up studies of endoscopic papillotomy of the sphincter of Vater by endoscopic examination in five out of 18 patients after sphincterotomy, which revealed important functional effects. "We found incomplete ablation of the sphincter," he said, "which accounts for the fact that after the procedure insufficiency of the muscle is present without stenosis, indicating that our method is producing the desired result."

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ONE
Fill external canal with the drops, with patient's head tilted at 45° angle;
TWO
Insert cotton plug and allow to remain for *only 15 to 30 minutes;*
THREE
Remove plug and gently wash ear with lukewarm water, using soft rubber syringe.
SIMPLE STEPS TO REMOVE EAR WAX
(USUALLY WITH A SINGLE 15-30 MINUTE TREATMENT)

- *Clears the ears* prior to ear examination, otologic therapy or audiometry.
- *Specific cerumenolytic action*—excellent results reported in over 90% of 2,700 adult and pediatric patients.*
- *Needs no repeated instillations* for several days, unlike some other agents.

Indications: Removal of cerumen; removal of impacted cerumen prior to ear examination, otologic therapy or audiometry. *Contraindications:* Previous untoward reaction to the drops; positive patch test. *Precautions:* Patch test in patients with suspected or known allergy. Use with caution in otitis externa; avoid using in otitis media, presence of perforated drum, known dermatologic sensitivity or other allergic manifestations. Avoid undue exposure of large skin areas to the drug. *Adverse Reactions:* Reported incidence in clinical studies* is about 1%, ranging from mild erythema to severe eczematoid reaction of external ear and periauricular tissue; all reported uneventful resolution and no sequelae. *Bibliography and detailed information available upon request. **Purdue Frederick**

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CERUMENEX DROPS
(triethanolamine polypeptide oleate-condensate 10.0% in propylene glycol with chlorbutanol 0.5%)

MBD Case History #1

1971 ...a difficult child, a distraught mother Medical diagnosis: MBD.

Robert Boynton,* second of five children, born October 7, 1963. Normal pregnancy and delivery.[1]

From the age of 3, Robert's mother found him "hard to handle," "wilder" than his brothers and sisters.[1]

At age 6, after an "extremely difficult" experience in kindergarten, Robert was referred to a pediatric neurologist. The examination and later psychological testing revealed a host of the neurologic "soft signs," plus an abnormal EEG.[1]

The diagnosis: average intelligence, but multiple signs of an underlying organic dysfunction.[1]

At age 7, Robert was placed in a special first-grade class called an "extended readiness program."[1]

Later that year, her child's continued problems at school and at home made Robert's mother "increasingly desperate" for help.

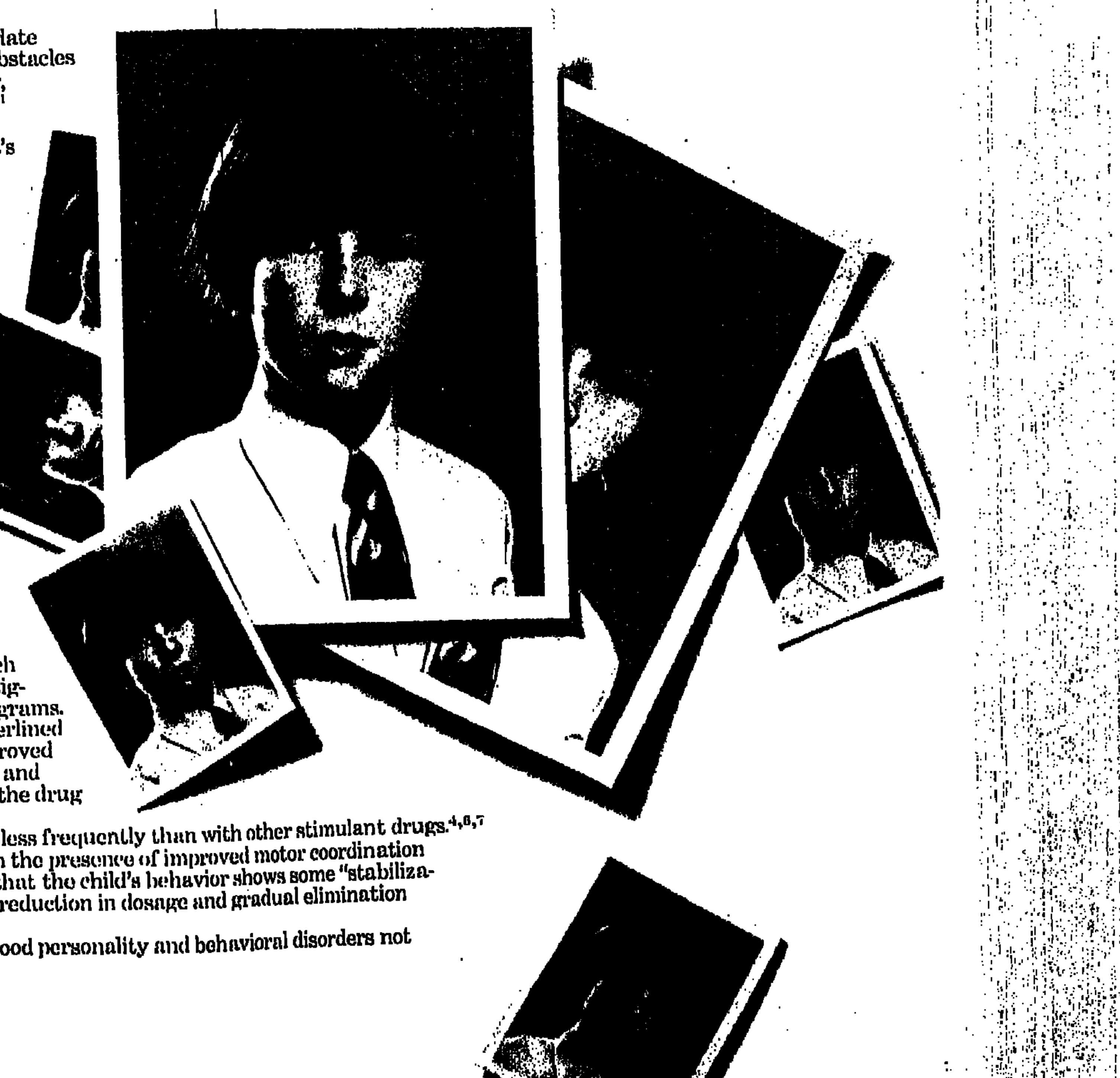
1974 ...a regular fourth-grader, accepted at home

In the opinion of the physician, methylphenidate (Ritalin) was called for to help the child over the obstacles of hyperactivity. So he initiated a trial of the drug, which was then implemented on school days only.[1]

The improvement in classroom performance and behavior was "prompt and dramatic." Robert's teacher could "scarcely believe" that he was the same child.[1]

For the past 4 years (as of April 1974), Robert has been maintained on 15 mg methylphenidate daily during school periods. During the summer he attends day camp and is not on medication. He is in a regular fourth-grade class, and behavioral problems at home have lessened. Robert's parents now find it much easier to accept their son.[1]

*Note: In this presentation, clinical material has been used factually with the permission of the physician. However, identities have been concealed and names changed.



How other children with MBD can benefit from methylphenidate therapy

Of course, medication is not indicated for all MBD children; nor will all such children respond to drug therapy.

However, when pharmacotherapy is clearly indicated, the use of a widely successful drug such as Ritalin (methylphenidate) may prove to be a significant element in many complete remedial programs.

Over a decade of controlled studies has underlined the beneficial effects of Ritalin in producing improved behavior ratings,[2,3] better motor coordination,[2,4] and cognition and learning.[2,4] Indeed, it is currently the drug of choice in many MBD situations.[5]

And side effects with Ritalin have occurred less frequently than with other stimulant drugs.[4,6,7]

Dosage should be periodically interrupted in the presence of improved motor coordination and behavior. These interruptions often reveal that the child's behavior shows some "stabilization" even without chemotherapy, permitting a reduction in dosage and gradual elimination of drug therapy.

Of course, Ritalin is not indicated for childhood personality and behavioral disorders not associated with medical diagnosis of MBD.

An MBD child on the road to maturity Ritalin® (methylphenidate) can help when medication is indicated

Ritalin® hydrochloride ©
(methylphenidate hydrochloride)

TABLETS

INDICATION
Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social)

Special Diagnostic Considerations
Specific etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

Characteristics commonly reported include: chronic history of short attention span, distractibility, emotional lability, impulsivity, and moderate to severe hyperactivity; minor neurological signs and abnormal EEG. Learning may or may not be impaired. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics.

Drug treatment is not indicated for all children with MBD. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is generally necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

CONTRAINDICATIONS
Marked anxiety, tension, and agitation, since Ritalin may aggravate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS
Ritalin should not be used in children under six years, since safety and efficacy in this age group have not been established.

Sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available. Although a causal relationship has not been established, suppression of growth (ie, weight gain and/or height) has been reported with long-term use of stimulants in children. Therefore, children requiring long-term therapy should be carefully monitored.

Ritalin should not be used for severe depression of either exogenous or endogenous origin or for the prevention of normal fatigue states.

Ritalin may lower the convulsive threshold in patients with or without prior seizures; with or without prior EEG abnormalities, even in absence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. If seizures occur, Ritalin should be discontinued.

Use cautiously in patients with hypertension. Blood pressure should be monitored at appropriate intervals in all patients taking Ritalin, especially those with hypertension.

Drug Interactions
Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy
Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence
Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS
Patients with an element of agitation may react adversely; discontinue therapy if necessary.

Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

ADVERSE REACTIONS
Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura); anorexia; nausea; dizziness; palpitations; headache; dyskinesia; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking this drug: leukopenia and/or anemia; a few instances of scalp hair loss.

In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

DOSAGE AND ADMINISTRATION
Children with Minimal Brain Dysfunction (6 years and over)

Start with small doses (eg, 5 mg before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. Daily dosage above 60 mg is not recommended. If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.

Ritalin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

HOW SUPPLIED
Tablets, 20 mg (peach, scored); bottles of 100 and 1000.

Tablets, 10 mg (pale green, scored); bottles of 100, 500, 1000 and Accu-pak blister units of 100.

Tablets, 5 mg (pale yellow); bottles of 100, 500, and 1000.

Consult complete product literature before prescribing. Rev. 3/73

References:
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CIBA Pharmaceutical Company
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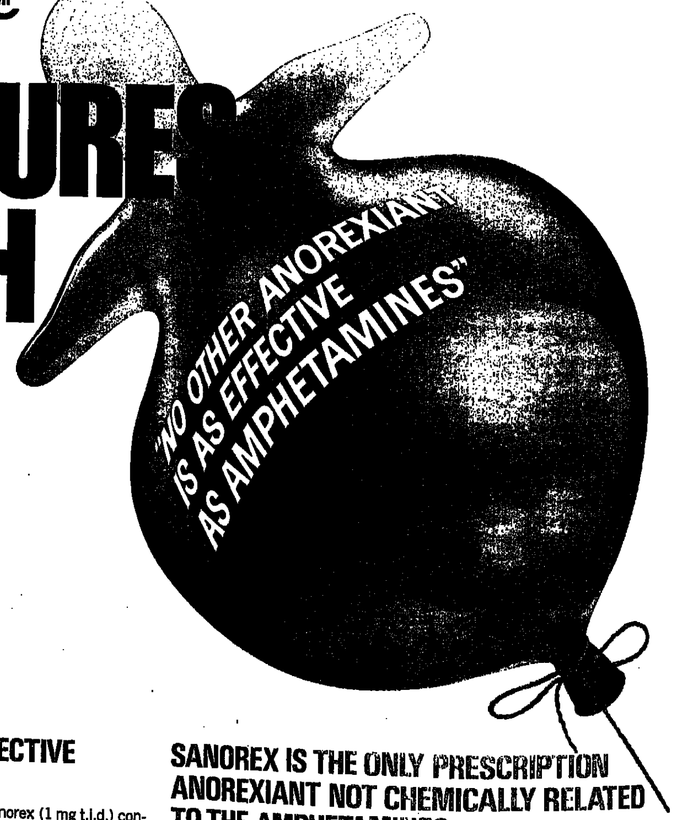
Summit, New Jersey 07901

CIBA

SANOREX®
(MAZINDOL)©
TABLETS, 1 mg and 2 mg

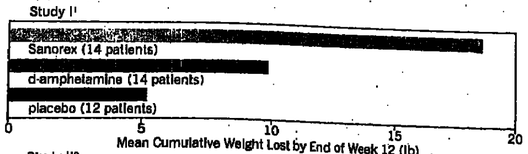
PUNCTURE A MYTH



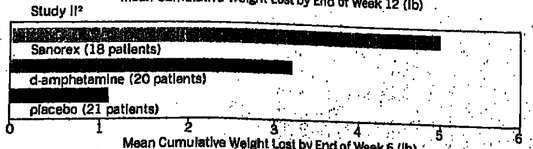
SANOREX IS AT LEAST AS EFFECTIVE AS d-AMPHETAMINE

These double-blind studies[1-3] show that not only is Sanorex (1 mg t.i.d.) considerably more effective than placebo in helping patients achieve weight loss—but in these studies Sanorex has equalled or surpassed d-amphetamine (5 mg t.i.d.) in clinical efficacy. (Copies of these three studies are available on request.)

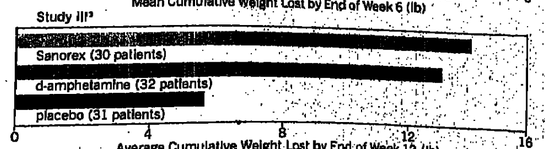
Study I[1]



Study II[2]



Study III[3]



SANOREX IS THE ONLY PRESCRIPTION ANOREXIANT NOT CHEMICALLY RELATED TO THE AMPHETAMINES

Although the pharmacologic activity of Sanorex and that of amphetamines are similar in many ways (including central nervous system stimulation in humans and animals, as well as production of stereotyped behavior in animals), animal experiments also suggest that there are differences.*

Different Chemical Structure
Sanorex is chemically unrelated to d-amphetamine—or any other "non-amphetamine" anorexiant available—and cannot be converted into an amphetamine-like substance in a biologic system.

Different Neurochemical Action*
Animal studies suggest that Sanorex, unlike d-amphetamine, does *not* interfere with norepinephrine synthesis.

Action of d-Amphetamine*
In animal studies, d-amphetamine (like food) activates afferent neurons leading to appetite centers in the hypothalamus. Resulting release of norepinephrine activates the receptor neurons. Unlike food, however, d-amphetamine also suppresses norepinephrine synthesis. Thus, increasingly larger doses of d-amphetamine become necessary to produce an effect.

Action of Sanorex*
After intake of food stimulates the release of norepinephrine from afferent neurons, Sanorex blocks its re-uptake without disturbing normal synthesis and release.

Simplicity and Flexibility of Dosage
Simple one-a-day dosage is facilitated by 2-mg tablets (taken one hour before lunch). New flexibility (for the patient in whom 1 mg t.i.d. is preferred) is now facilitated by new 1-mg tablets (taken one hour before meals).

*The significance of these differences for humans is uncertain.

For Brief Summary, please see facing page.

SANOREX®
(MAZINDOL)©

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3. Varnes BJ: Practical considerations for managing obese patients: Initial interview and effective treatment in the office. Scientific Exhibit presented at the American Medical Association, 27th Clinical Convention, Anaheim, Calif., Dec 1-4, 1973.

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.
Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).
Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.
Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given pressor amine agents (e.g., levarterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.
Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdosage or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.
Usage in Pregnancy: In rats and rabbits an increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses. Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.
Usage in Children: Not recommended for use in children under 12 years of age.
Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.
Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. *Cardiovascular:* Palpitation, tachycardia. *Central Nervous System:* Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. *Gastrointestinal:* Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. *Skin:* Rash, excessive sweating, clamminess. *Endocrine:* Impotence, changes in libido have rarely been observed. *Eye:* Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.
Dosage and Administration: 1 mg three times daily, one hour before meals, or 2 mg per day, taken one hour before lunch in a single dose.
How Supplied: Tablets, 1 mg and 2 mg, in packages of 100.
Before prescribing or administering, see package circular for Prescribing Information. 74-374 SANDOZ
SANDOZ PHARMACEUTICALS, EAST HANOVER, N.J. 07936

One Man . . . and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune

'The Good Poles'

Dear Dr. Sackler:

LET ME REMIND you of some historical facts.* Up to September 1, 1939, nearly six million Jews lived in Poland. They shared with the Poles both the poverty of the country, as well as the ability to pursue their own particular cultural attributes.

All of this came to a tragic end that September not because of any specific set of circumstances in Poland but purely because, due to Munich agreements and other encouragement of the West which allowed Hitler to expand into the East, Poland was overrun by Germany. The American Ambassador in London (at about that time) stated that he would not wish one English pound spent or one English soldier killed for the sake of Poland. (See Bethel's *The War Hitler Won*).

After the invasion, Western Poland was incorporated into Germany, Polish schools were closed, Polish art treasures stolen, Polish professors (Pole and Jew alike) arrested. The Polish Jews undoubtedly suffered but it must not be forgotten that over three million Poles who were not Jewish were also murdered. Polish children were abducted if they met certain racial Aryan classification, a crime which is as horrendous as any in our history. Over a million and a half Poles were taken to Russian Siberia by the Russians who had been partners in Hitler's perfidy. They were taken there for purposes of hard labor and liquidation!

The Polish Underground Army attempted to protect Jews and Poles alike! If it failed, and it did fail, it was because it failed in every respect. The Western Allies refused to drop the agreed number of arms to Poland. They refused General Sikorski permission to have its own long range supply planes. The British were always in control.

During 1939-45 the genocide practiced against the Poles and the Jews was complete. In your editorial you remarked about the memorial in Jerusalem, but you fail to comment that many (in fact 50 per cent) of the names so honored are of Poles. You fail to realize that, unlike the situation in other countries like Denmark, assistance to a Jew meant instant execution.

Jews have shared with Poles for many centuries mutual history, tragedy as well as happiness. I hope that in view of your concern for good conscience and principle, you will have the objectivity to put this letter in your TRIBUNE.

MICHAEL A. PESZKE, M.D.
Associate Professor,
Director, Psychiatric Outpatient Clinic
University of Connecticut
School of Medicine
Farmington, Conn.

*Referring to Dr. Sackler's column, "Is This How a Conscience Dies," MEDICAL TRIBUNE, June 11, 1975.

IN YOUR column "Is This How a Conscience Dies," you seem to be perpetuating the somewhat inaccurate and slanted opinion of anti-Polish feelings. There are fortunately some new books in English on the subject of help and sacrifice of the Polish population during the holocaust being published. They may be purchased at the Kosciuszko Foundation, written by Poles of Catholic or Jewish faith:

1. *The Blood Shed Unites Us*, by Wladyslaw Bartoszekski.

2. *The Samaritans: Heroes of the Holocaust*, by the same author.

3. *He Who Saves One Life*, by Kazimierz Iranek-Osmecki.

I am very surprised that you have not seen at Yad Vashem, the memorial and names of Polish nationals.

In summary, to answer your rhetorical question, "Where were the good Poles?" I would answer, they were helping their Jewish compatriots, they were exterminated in gas chambers, just as rapidly (3 to 4 million) or they were fighting on all fronts to eliminate the Nazi menace from the beginning to the end of the war.

I hope that my few comments will be of help to you, especially when you are writing about conscience.

WITOLD KAWECKI, M.D.
New Britain, Conn.

Dear Drs. Peszke and Kawecki:

In the column referred to I sought to point the finger not at others, but at myself and at all who lightly indict others without realizing how easy it would be to be indicted. I have believed in the past and still do that there were good Poles as well as good Germans and good French.

The omission in my column is unjustifiable for the essence of my belief is that goodness is not restricted to any one nation, to any one race or to any one color. May I salute the Poles who are commemorated in the Avenue of Righteous in Jerusalem and the many others not named but whom they represent. And may I express my thanks to them, to Dr. Witold Kawecki and Dr. Michael A. Peszke for making clearer the point I had hoped to convey—that there is no monopoly of evil by any one people and no monopoly of goodness either.

It is too easy to lull our conscience, first in matters of little moment, and then on subjects of great principle.

A.M.S.

Medicine on Stamps

Moynier, Dunant, Dufour

Issued by Monaco on May 3, 1963, to commemorate the centenary of the International Red Cross, the stamp shows three of the men responsible for its founding. Gustave Moynier, first president, also founded the Institute of International Law. Guillaume Dufour served as chairman of the Geneva Convention.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

Low Doses of Insulin Are Found to Correct Acidosis in Diabetics

By MICHAEL HERRING
Medical Tribune Staff

NEW YORK—Low-dose insulin therapy is effective in correcting diabetic ketoacidosis, according to a 42-patient study reported to the American Diabetes Association here by Dr. Abbas E. Kitabchi.

The regimen proved simpler than conventional high doses of insulin, "without the risk of hypoglycemia," he said.

Dr. Kitabchi, who is Professor of Medicine and Biochemistry at the University of Tennessee Center for Health Sciences, said moreover that he found no clinical evidence to support the notion that patients with diabetic ketoacidosis (DKA) are "insulin-resistant" and require higher doses than diabetics without ketoacidosis.

Through last March, he related, the study has included 18 DKA patients on a high-dose (HD) insulin regimen (40 to 150 units, based on initial plasma glucose) and 24 on a low-dose (LD) regimen of 0.1 unit of insulin per pound of body weight.

Patients were randomly selected for low- or high-dose treatment. There was no significant difference in the biochemical profile of either group before treatment, Dr. Kitabchi noted. The total group comprised almost all DKA patients in the hospital and provided "an accurate profile of the DKA patient."

In the HD group, insulin was administered both intramuscularly and subcutaneously. The LD patients received only I.M. insulin.

"Insulin resistance" was measured by the rate of glucose drop, determined hourly, and "if plasma glucose had not dropped by 10 per cent, the initial insulin (HD or LD) was repeated [after each hourly check]," Dr. Kitabchi said.

The decision to conduct the test was influenced by the current shortage of insulin, Dr. Kitabchi noted.

Venkachalam Ayyagari and Sonia Guerra assisted in the study.

Poll Finds 53% of MDs Favor Euthanasia for Trisomy 18

Continued from page 1

The study, done at the University of California School of Public Health at Berkeley, was reported to the annual meeting of the Canadian Pediatric Association here by Dr. Helen R. McKilligin, now Assistant Professor, Maternal and Child Health, Memorial University, St. John's, Newfoundland.

A total of 137 physicians responded to the questionnaire. There were no significant variations between the opinions of pediatricians or obstetricians, nor were there differences based on age or sex of the respondent. But there was a statistical difference on religious affiliation.

The Key Question

The key question, Dr. McKilligin said, was: Given complete anonymity and no constraint by existing laws, indicate which of the following statements comes closest to the response you would prefer the family to make regarding management: "Everything humanly possible," "Care, but nothing heroic," "Withhold all treatment including surgery," "End the suffering quickly."

The physicians were asked to apply the statements to these five clinical situations:

- Down's syndrome with no lethal complications.
- Myelomeningocele with moderate neurological impairment.
- Hydrocephalus present at birth.
- Down's syndrome plus intestinal obstruction.
- Trisomy 18.

Although only 22 per cent favored active or passive euthanasia for Down's syndrome, 50 per cent favored it for Down's syndrome with intestinal obstruction. Dr. McKilligin commented: "This shows that some physicians chose to view a relatively simple operation as an insurmountable barrier and so excuse their apparent change of attitude. This probably reveals their subconscious feeling against prolonging the life of an abnormal conceptus."

About one-third of the physicians stipulated a religious affiliation and they were much less inclined to favor active or passive euthanasia. For example, 57 per cent of those with no religious affiliation favored it for hydrocephalus at birth, compared to only 43 per cent in the other group.

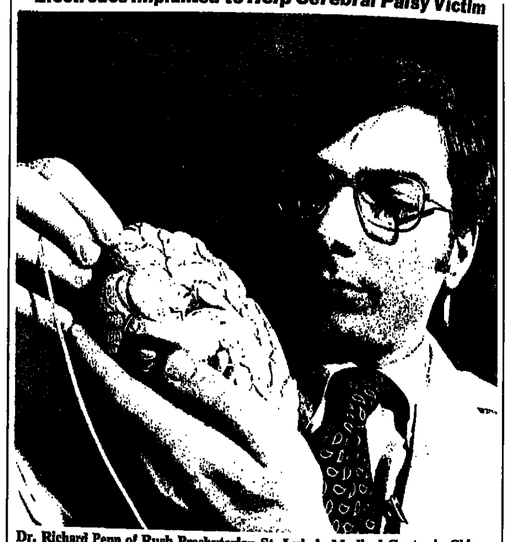
Dr. McKilligin noted that the majority of physicians "fall into the limbo of indecision."

"Should we be content with the ambivalent attitude of default which presently permeates the professional management of severe congenital anomaly at birth?" she asked.

In her own unit, she said, there is a whole spectrum of attitudes. "Life becomes very difficult, very unhappy. You will find a nurse spending 1½ hours trying to feed a baby. You'll find a physician who says 'Stop all oral intake and let the baby die as soon as possible.' You find another physician who says 'We should put down a lavage tube to keep the baby alive.' You find there are no guidelines and you really are at a loss. The parents suffer. It is a very difficult and thorny problem."

Co-author was Dr. Howard Diller.

Electrodes Implanted to Help Cerebral Palsy Victim



Dr. Richard Penn of Rush Presbyterian St. Luke's Medical Center in Chicago holds a model of a brain and shows where he implanted electrodes in a seven year old boy suffering from cerebral palsy in an attempt to enable the child to control his arms and legs.

MDs Are Increasing Patient Fees to Cover Malpractice Costs

Medical Tribune Report

NEW YORK—Among the "tremendous changes in the practice of medicine" brought on by the malpractice crisis is a "greater expense to the consumer" for health care services, according to Dr. Alexander Levine, past Chairman of the New York State District Branch of the American Psychiatric Association.

"Limiting his practice and paying exorbitant malpractice insurance premiums lowers the income level of the average physician, especially the specialist, and as a result patients' fees will be higher, which will in turn create more resentment and hostility on the part of the complaining patient and perhaps increase chances of a malpractice suit," Dr. Levine told a recent meeting of psychiatrists at Downstate Medical Center, Brooklyn.

The situation, in his view, is "intolerable." The recent plethora of malpractice suits (one out of every ten doctors has been or is being sued, he noted) has destroyed the basic intimacy of the doctor-patient relationship, so that "a malpractice suit is less objectionable than it might have been formerly."

Other changes in medical practice cited by Dr. Levine were:

- Fear of responsibility. Doctors will start to see patients as adversaries, rather than people who need help.
- Cautious treatment. More tests, less human judgment drives up the cost of health care and is "not necessarily more efficient."
- Early referrals and hospitalizations. Any disorder the doctor feels uneasy about will be promptly referred to a specialist. Furthermore, "minor surgical procedures will no longer be done in the physician's office."
- Early retirements. Most physicians will tend to retire as soon as they can, "rather than continue practicing in a profession which is under pressure.
- Less private practice. "Young doctors will be reluctant to enter private practice and will seek employment in hospitals.

Coiled Shunts Implanted in 3 Hydrocephalics

Continued from page 1

poor prognostic outlook. It's too early to say that any [of the shunts] will work after the passage of years," they added.

"We anticipate that complications will arise, as they do in all shunting procedures, and it remains to be seen how difficult the management of such problems will be," they said.

Cephalic Incision Made

After a cephalic incision, the procedure continues with insertion of a brain-ventricular catheter attached to a Pudenz flush pump, a burr hole in the skull large enough for the reservoir of the pump having been rongeured out. The distal limb of the flush pump is temporarily occluded.

An incision is then made in the third intercostal space and a Silastic pouch, containing eight extra inches of coiled atrial catheter, is placed behind the thymus and fixed to the pericardium with vascular staples.

The distal one inch of the atrial catheter containing a slit valve is then inserted in the right atrium through a small purse-string suture, which is tied down over a firm plastic collar located one inch from the catheter tip. The proximal end is passed up through the chest apex and by means of a small connecting neck incision pulled up from the chest and passed up to the cephalic incision through a "subcutaneous tunnel" in the neck. It is then connected to the distal limb of the Pudenz pump over a plastic connection. Because the Silastic is noninteractive, the surgeons noted, somatic growths or scar tissue around the pouch are unlikely.

Survivors 'Doing Well'

The three surviving infants, all less than three months old at operation, are "doing well and the shunts are functional" at six, 12, and 14 months postoperative, the surgeons reported. While they were unwilling to make any projections on the mental status of the children, Dr. Milhort was optimistic that "two of these kids will be fine." However, both emphasized that it is too early to be sure.

Though they still regard the results as preliminary, they now plan to perform about 10 coiled-shunt operations annually, while continuing close follow-up on the original patients.

Other Designs Noted

They also mentioned the efforts of others to develop designs for telescopic or accordian-like catheters to serve as permanent shunts in growing children.

To point up the need for a successful elongating shunt, the surgeons cited results with replacement-shunts at their own hospital: of the 40 children who first had this kind of surgery at Children's Hospital 10 years ago, only three are alive at present.

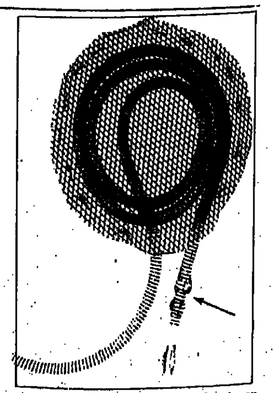


Photo of thoracic limb of direct cardiac shunt shows prefabricated Silastic pouch containing three coils of tubing and atrial catheter that has a plastic collar one inch from the tip (arrow).

A Medical Tribune Encore

Confessions of a Physician With Hay Fever

With a Short Note on What to Do About It

By DONALD J. DALESSIO, M.D.

Head, Division of Neurology, Scripps Clinic and Research Foundation, La Jolla, Calif.

No Ka-choo Here, Ex-sneezer Says

In the August 22, 1973 issue of MEDICAL TRIBUNE, on page 14, you published "Confessions of a Physician with Hay Fever with a Short Note on What to Do About It" by Donald J. Dalessio, M.D. I wish you would publish it again this August ...let me tell you why.

Since my internship 13 years ago, I have told my colleagues that if they would cure me of my August-October hay fever, I would give them a $1,000 on the spot. Since I was 5 years old I have avoided vacations in the fall and have experienced desensitizations, antihistamines, and constant air conditioning. And, having completed my training in both internal medicine and psychiatry, I have not found any evidence for psychosomatic factors in myself, save perhaps a worsening of symptoms with excess fatigue.

However, since taking Dr. Dalessio's advice—even modifying it to applying fluocinonide 0.05 per cent every two-three days and without Polaramine®, I have been completely free of any symptoms whatsoever. Only fellow hay fever sufferers will understand the true significance of having dry handkerchiefs from August to October (even during the stress and excitement of taking and passing my Boards in Psychiatry in October of 1973).

Dr. Dalessio and I have exchanged letters and while I have sobered regarding the $1,000, I've already sent him an equivalent amount of my appreciation. I hope you'll republish the article—you performed a real service for me when you did several years ago.

PETER B. BLOOM, M.D.
Philadelphia

OF ALL THE RELATIVELY SMALL ILLS that afflict mankind, surely none is more annoying than allergic rhinitis.

Consider the following scene. After a long winter, cold, wet, and dull, comes spring, when all men's fancies turn—sunny days, the long, lovely twilights. But with it also comes a veritable pollen explosion and, for those of us who are sensitive, burning eyes, tickling palates, sneezes, and rhinorrhea. Only those who have suffered through seven or eight repeated wild sneezes know what this means.

I have assured myself over the years that there must be some biologic advantage to this devil's curse, for Mother Nature couldn't be so perverse as to do this to her children without a reason. Not Mother Nature! Unfortunately, however, no such proof of advantage can be found. I comfort myself with the thought that someday someone will discover that respiratory cancer is less common in those with allergic rhinitis.

As a child I was not troubled by this problem. I was addicted to baseball and remember spending long hours in the grassy plains of New Jersey without difficulty. Not until my last year of college did I realize that something was amiss, for in the spring of that year I suffered with chronic nasal catarrh, paroxysmal sneezing, and tickling of the palate, symptoms I have come to recognize so well in the last 20 years. I reported first to the college infirmary but was dismissed out of hand by the nurse because I had no fever. It was only after several months that I began to understand my symptoms.

Each year since, in late April and early May, the symptoms begin, raging through May, June, and July and beginning to taper in August. I am allergic to trees and grasses but can stand unafraid in a field of goldenrod, so that, by September, I am cured again. No wonder I love autumn.

Geography makes a great difference in the degree of symptoms, though nothing is truly as international and democratic as pollen antigens. In areas where grasses and trees abound and where there are four seasons, the late spring and early summer are devastating. I have been as miserable in France as in Connecticut. A decade or so ago I moved to southern California and for several years, perhaps five, was free of symptoms. But soon the thing overcame me again, less severe than formerly but more prolonged in terms of months, related perhaps to a lower but more persistent level of inhalant pollens. Whether it is better to be seriously bothered for two or three months or chronically annoyed for five to six months is a dilemma I cannot resolve.

The Empathy Flows

As the years have passed I have questioned my neurological patients about allergic rhinitis, primarily for my own information. You cannot imagine the empathy that flows back and forth from physician to patient when both discover that they have hay fever. I had hoped to find that allergic rhinitis became less troublesome as I aged, much in the manner of migraine or, perhaps, the reduction in petit mal attacks. Sadly, even though other appetites may fade with age, the ability of the nasal and other mucous membranes to gorge themselves on allergens appears to withstand the assaults of time.

I have consulted allergists on occasion, of course. I admire them greatly, but usually their response to my complaints is stereotyped. They want to skin-test me and administer biweekly injections of pollens to which I am allergic, which would expose me to anaphylaxis or some other—though less violent—reactions to antigenic stimuli, and I am not pleased. The thought of being injected with a host of impure foreign antigens has always frightened me, and hence I have avoided hyposensitization therapy. Also, I must consume quantities of medicine, including antihistamines, which dull me, and anticongestants, which make me anxious. The chronic use of sedatives has even been suggested, a regimen which would be certain to make me more torpid than the ailment itself.

Usually, being opposed to any medicine other than aspirin and my spouse's chicken soup, I wait out the symptoms, armed with Kleenex, paper towels, or whatever else is available, and a hope that better days are ahead.

I have also surveyed all the usual sources regarding therapy, but have been little impressed by them. Hence it is with trepidation that I offer the following hints on the management of allergic rhinitis. The recommendations are based on a series of one (D.J.D.). No double-blind control studies have been done. Toxicology has not been performed. I can only say that if it works for me, it may work for you.

If the nasal symptoms of allergic rhinitis can be suppressed, then the conjunctival and palatal itching will be much less troublesome. Hence, on awakening each morning I apply a small amount of potent corticosteroid cream with my fifth finger to the nasal mucous membranes in the region of the inferior turbinates. Either flumethasone, 0.03 per cent, or fluocinonide, 0.05 per cent, can be used. Only a small amount is necessary, and one need not be messy. The application of the cream causes slight nasal irritation, and often then I snuff vigorously, inhaling the material to the upper reaches of the nasal mucous membranes. At night this process is repeated. Also at night, before retiring, 6 mg. of Polaramine® is used. And that is all. The nocturnal antihistamine provides antihistaminic effects at night, when pollen counts rise and when the sedative side effects are not important. It represents a rational adjunct to the therapy.

The results are gratifying. Some occasional sneezing still occurs, and nasal and oral pharyngeal tickles may appear through the day, but rhinorrhea is much reduced and paroxysmal sneezing is almost eliminated.

Some Objections Countered

One can foresee objections to this program, particularly the use of an intranasal corticosteroid cream. It may be absorbed into the body, or it may predispose one to localized infection in and about the nares. To the first objection I would say that the amounts of corticosteroid cream used are small, probably too small to produce parenteral effects. To the second, I can only observe that localized infection has not occurred. Indeed, the reduction in accumulated intranasal concretions and debris tends to reduce nasal picking and thereby reduces the introduction of staphylococci and other skin pathogens into the nares.

wine talk

By JOHN CHAMBERS
Author and Consultant to Morrell & Company, New York Wine Merchants

Italian Wine

Italian wines have come of age. Slowly but surely the wine-buying public is realizing the range and quality of Italian wine currently available. Better grape selection, more careful wine-making, increasingly stringent government regulation; all these are in part responsible for the dramatic improvement in Italian wines, but even more important has been the rise in French and German wine prices. This rise created a vacuum—and suddenly there was a market for Italy's best wines. How good are they? Measured on a scale of value for price, they are probably the best bargains in the wine world today.

Italian red wines can be divided into three groups. The first (which somewhat resemble French Rhones) are big, rich, sturdy, tannic wines, many of them made from the nebbiolo grape or its near relations in the northwest corner of Italy. Some of the names to look for are *Barolo, Barbaresco, Gattinara, Spanna, Ghemme, Inferno, Sassella, Grumello, Freisa,* some *Barbera,* and some *Dolcetto.*

Age Is a Factor

These wines should be at least seven years old, and in the case of the first five, preferably older, and they should be opened 1-2 hours before they are to be drunk. A second group, the *Chiantis,* bear some resemblance to the wines of Bordeaux. As in the case of clarets, the inexpensive ones can be drunk young, but the better grades should have at least six years of age and should be opened an hour before they are to be drunk. In addition to the Chiantis, wines which fit into this category are *Valpolicella, Torgiano, Cabernet, Valgella, Corvo Red, Santa Maddelena,* and *Caldaro.*

The lightest group of Italian reds, an equivalent of Beaujolais and Cotes du Rhone, are a mixed bag from all over Italy, of which the best known is the Veronese *Bardolino,* followed by *Merlot,* the less expensive *Chiantis, Barberas,* and *Dolcettos, Montepulciano* from Abruzzi, *Rosso Piceno, Gragnano,* and *Segesta* from Sicily.

Italian white wines do not match the quality of the finest reds, but they can be very good. Names to look for include *Soave, Corvo Bianco, Pinot Grigio, Frascati, Verdicchio, Orvieto, Lugana,* the white wines of the major Chianti shippers, *Verduzzo, Tocai,* and any of the white wines from the Italian Tyrol. Italian roses are generally dry, sturdy, well-made wines which go well with summer red meat cookery. Probably the best is the *Chiaretto* of Lake Garda, followed by the *Ravello Rose* of Caruso and the *Rosatello* of Ruffino.

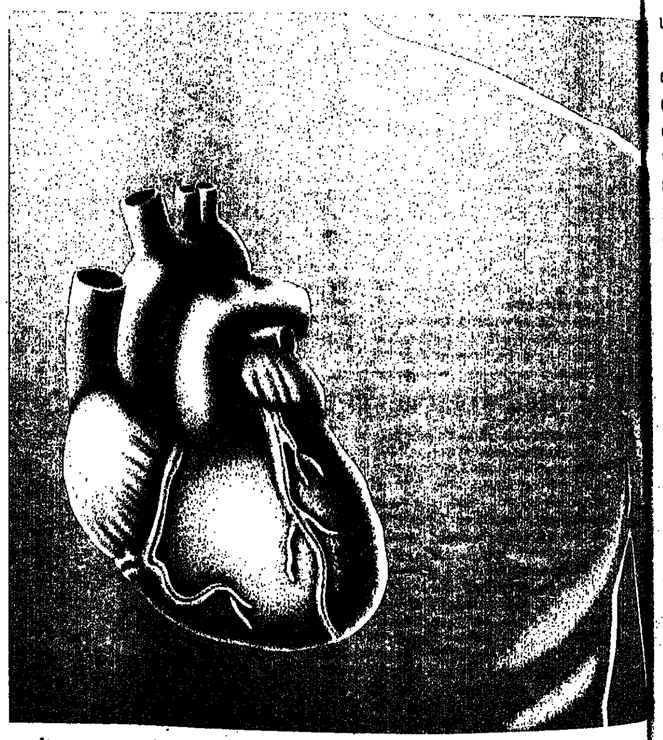
Next Month: M.D. Winemaker Extraordinaire

HOW MUCH ANXIETY IS PRODUCTIVE IN THE CARDIAC PATIENT?

Approximately 70% of deaths caused by acute myocardial infarction take place before the patient reaches the hospital.[1] Delay in obtaining medical care is cited as a major cause for this high incidence, and denial may contribute to this delay.

This denial in the cardiac patient is a more obvious aspect of anxiety that is *not* productive. There are others; for example, the previously self-reliant patient who, on finding himself suddenly dependent, reacts with hostility, refuses to cooperate and thus causes serious problems during the intensive care and early rehabilitative stages of his hospitalization.

Even more common, perhaps, is the postcoronary patient who fears a return to work and other everyday activities. The basis for this "cardiac neurosis" is the patient's notion that activity itself is life-threatening.[2]



When anxiety is productive

A certain amount of anxiety in the cardiac patient is both realistic and normal. And in some patients can be productive. In the acute phase of the disease, anxiety can prompt the patient to seek immediate medical attention. Later, it can encourage cooperation during hospitalization.

In the rehabilitative phase, productive anxiety can help a patient adhere to a possibly difficult medical regimen: to eat properly, to exercise in a manner compatible with his capacities, to alter habits such as smoking. Productive anxiety can hasten recovery—even prolong life.

Channeling anxiety into productive areas

Because unresolved anxiety can lead to psychologic defense mechanisms such as denial which may worsen the cardiac condition, open and ample discussion between physician and patient must be maintained and encouraged. In this way, the patient can verbalize his fears and the physician can help alleviate the patient's anxiety through reassurance and counseling.

Librium®(chlordiazepoxide HCl): often an excellent adjunct to your reassurance and counseling

Although the physician may attempt to help the cardiac patient cope with varied emotional problems through reassurance and counseling, excessive anxiety may persist. In this case, you may wish to consider the use of Librium adjunctively.

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Although clinical studies have not established a cause and effect relationship, you should also be aware that variable effects on blood coagulation have been reported very rarely in patients receiving oral anticoagulants and Librium.

References: 1. Zohman BL: *Geriatrics* 28:110-119, Feb 1973.
2. Keegan DL: *Can Fam Physician* 19(3):66-68, Mar 1973.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients, and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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BASIC WHEN ANXIETY AGGRAVATES ORGANIC DISEASE

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Infant Mortality Declines in North Vietnam

Medical Tribune World Service

GENEVA—Since 1945, infant mortality in North Vietnam has dropped from 300-400 per 1,000 to 26 per 1,000, according to Dr. Hoang Dinh Cau, that country's chief delegate to the World Health Assembly here. The number of hospital beds has risen from 4,000 to 40,000, he said, and there is a physician or medical auxiliary for every 4,000 persons.

This progress, he observed, has been achieved during three decades of war.

Dr. Cau, whose administration is now taking over responsibility for health care in South Vietnam, told MEDICAL TRIBUNE that the medical system has been built up on a strongly decentralized basis.

The key to the delivery of health care in his country, he explained, is the *poste sanitaire*, a village health center staffed by a medical auxiliary, a midwife, and two nurses and serving a community of 2,000-3,000 persons.

After initial training, he explained, the auxiliary works in his village for five years. Then he is sent for a three-year course of further training, which includes both Western and traditional medicine. At the same time, other students are taken from secondary schools for the formal medical course, which lasts six years.

The more gifted among the latter, Dr. Cau continued, are promoted to the district centers, which coordinate groups of 20-25 villages, or to city hospitals, but a considerable number return to general practice.

"We have no problem of brain drain," he declared. "These are village children, whose medical schooling is financed by their community, and they return to their village when they graduate."

Dr. Cau, a surgeon with considerable war experience, told MEDICAL TRIBUNE that the system of village health centers largely evolved to cope with wartime conditions. With road and rail transport cut by bombardment, there was often no access to central hospitals, and so the wounded were treated on the spot, where possible, by the *poste sanitaire* teams.

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For swabbing injection sites, minor wounds and sutures

Tribune Economic Analysis

The Price Break In White Bread Is a Bad Omen

BY LEON TANEWAY
Consulting Economist

The better the American economy performs, the less important the bread business is in the general economic scheme of things. Anytime bread happenings make business news, something's up inside the American economy. Few indicators could be worse than the break in the price of white bread in certain key metropolitan centers—Seattle, for example.

The white bread price war in Seattle shows how cannily the consuming public has been sitting out the businesses selling to it. It also shows how electric the response of consumers may be as soon as they win the bargains they're waiting for. Loaves offered at three for 99 cents went begging; but ads of a dime a loaf and rumors of a nickel a loaf in the offing spurred stampedes reminiscent of the shortages that greeted the outbreak of war in 1941.

These white bread bargains may prove tricky. All year long, the grain-processing industries and the food-distributing businesses dependent on them have been eking out margins on the price break in the grain and related meat markets. This break has taken a sharp toll on meat, poultry, dairy, and egg supplies. Consequently, these prices are shooting up again.

The basic markets are signaling a return to runaway food prices for America just when the reversals suffered in the bread business are pointing to the country's need to budget for a spell of relief from dietary inflation. This does not augur well for recovery prospects inside America.

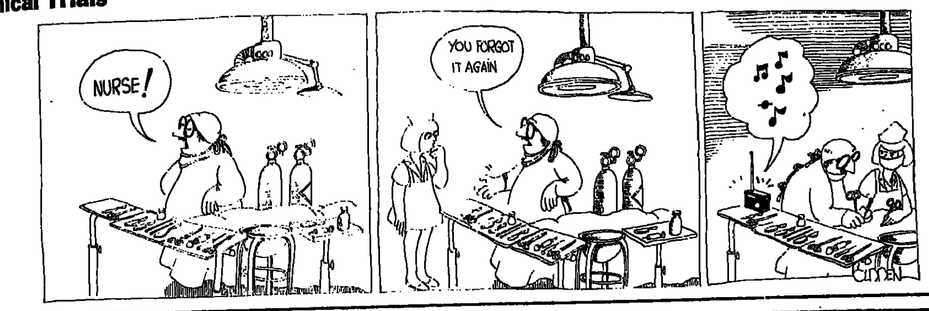
I have one life insurance policy ($20,000 modified whole life) which with inflation looks like peanuts for my family now, although it seemed respectable in 1947 when I purchased it. To it I have added another $100,000 policy. Now I'm considering cashing in the $20,000 policy and using the money to invest in local real estate lots. I expect them to be valuable in ten or twenty years, and a better form of insurance than inflatable money. Am I right? I liquidated about $35,000 in stocks which were nowhere near what I paid for them, and put that money into Treasury bills. But the change in interest rates makes me feel I ought to go into municipal bonds which seems more stable. Or am I wrong?

Iowa M.D.

Your temptation to cash in your insurance for local real estate lots is not right because premature. Undeveloped real estate values are vulnerable to illiquidity pressures. Your hankering after municipal bonds is wrong if you are thinking of any with maturities of more than two years. The same unfavorable money pressures responsible for making stocks too risky to handle are hurting market values of bonds with longer maturities.

Clinical Trials

by Oldden



TRIBUNE SPORTS REPORT

Drug Tests Will Be Performed On Athletes at '76 Olympics

Medical Tribune Report

MONTREAL—Officials at the 1976 Olympic Games, to be held here next July, have approved measures to test participants for the presence of drugs intended to improve performance and to screen all women athletes for X-chromatin.

The medical commission of the Olympic's International Organizing Committee (I.O.C.) announced the ratification of so-called "doping" and "femininity control" tests. The first four placers in each event, and other competitors selected at random, will provide urine samples to be assayed at an Olympic laboratory constructed at a cost of $250,000.

Special attention will be given to anabolic steroids, used mainly in sports where weight gives an advantage, such as the discus.

"Remarkable progress has been made in the past few years on steroid detection," Dr. Albert Dirix of Belgium, an I.O.C. member, said. "We can now detect most of them using only a urine sample."

Prince Alexandre de Merode of Belgium, head of the I.O.C.'s medical commission, agreed that there should not be any real problem with most steroids, but he said that several new types are available for which adequate tests have not yet been developed.

Forbidden Drugs Listed

"We hope that such tests will be developed by 1976," he said.

Other drugs forbidden by I.O.C. includes the amphetamines and related compounds, some central nervous system stimulants, sympathomimetic amines (such as ephedrine), narcotic analgesics, and alcohol. Amphetamines and ephedrine in the form of nasal drops are said to be the drugs most frequently used by athletes, although it has not been proved that they do anything more for them than mask fatigue.

Blood sampling to detect alcohol consumption by athletes who wish a depressant to steady their nerves will also be undertaken. The blood analysis will have to show a zero reading.

Screening for all these agents will require the largest deployment of medical staff in the history of the Olympics. Two hundred and fifty physicians will be assisted by some 2,000 technicians and other personnel, and a collection station for urine and blood samples will be set up at each competition site.

As a screening test of all participants in the women's events, the determination of X-chromatin will be conducted on a smear of buccal mucous membrane. If the test is inconclusive, further tests of Y-chromatin determination in blood smears, chromosome analysis in blood samples, and gynecological examination will be mandatory.

A Future Doctor

Dave Gaudin, who lost both legs due to congenital birth defects, hits a golf ball as his wife looks on. But most of Dave's time is spent "hitting" the books at medical school where he is studying to be a doctor.

National Health Insurance Is Viewed As Changing MD-Patient Relations

Medical Tribune Report

BROOKLYN—How will national health insurance, when and if it comes, affect the practice of medicine? Whether results are positive or negative "depends on how this is legislated," according to Dr. Julius Buchwald, Clinical Assistant Professor of Psychiatry at the State University of New York College of Medicine here.

"It could go either way," he told a meeting sponsored by the American Academy of Family Physicians and the Brooklyn Psychiatric Society at Downstate Medical Center.

Dr. Buchwald found few reasons, however, for doctors to be optimistic about the prospect of nationalized insurance, and his list of negative possibilities was far weightier.

On the positive side, he cited the wider range of social, ethnic, and economic groups a physician may see in daily practice if everyone has health insurance.

"This will enrich our clinical experience," he observed, "as well as our knowledge and understanding of public health."

Moreover, national health insurance could provide greater financial security for some physicians, he said.

On the other hand, Dr. Buchwald continued, loss of control over fees would represent an infringement of the classic doctor-patient relationship.

The Fee Says 'Thanks'

"The fee is part of this relationship," he commented. "It can be as intimate as a handshake in good patient relations, a way of saying 'thank you' that will no longer be available to the patient. . . .

"You may think that the set fee is enough—but *you* didn't decide it. It represents the loss of a freedom doctors have always had."

A more serious problem, he went on, would arise in situations where prejudice exists: "Prejudiced physicians should not treat people they're prejudiced against. However, with national health insurance, they may be required to treat whoever walks through the door."

Dr. Buchwald also said that when the physician will be working for the Government, the all-too-familiar inequities of Federal administration will be passed on to the doctor and his patients.

"The Government has an enormous credibility gap, with its blacklists, investigations, and so on," he said. "Suddenly, this same Government is the doctor's employer."

IMMATERIA MEDICA

The Raggedy Ann Story

• You're probably too young to know but the dolls, Raggedy Ann—and Raggedy Andy—were actually invented by an artist-writer named Johnny Gruelle in 1910 to promote the sale of his illustrated books on their adventures. It's still a family business, doing $13 million a year, and the books still read: "Raggedy Ann and Raggedy Andy turned over and over as they fell. . . . It was quite dark, but that does not worry them, for both Raggedy Ann and Raggedy Andy have bright little shoe-button eyes. One can see very well with shoe button eyes if one is a rag doll stuffed with nice, clean, white cotton." —from *Raggedy Ann in Cookie Land*.

That's about a billion light years away from the slam-bang violence of TV cartoons for kids today—POW! went the puddycat! No wonder the kids love *Sesame Street*.

ITT is producing a Raggedy Ann movie next year, but we're not guaranteeing anything except maybe that you read it here first. A first-class maybe guarantee, that is.

It's Immaterial

• *Teacher:* What is the difference between the body and the soul?

Johnny (vacantly): The body is mortal and material; the soul—

Teacher (impatiently): Yes, and the soul?

Johnny: The soul is immortal and immaterial.

We wouldn't have mentioned it at all but that was written by George Santayana for the Harvard *Lampoon* when a student—and long before he became known as a philosopher.

It's only fair to report that he also wrote: "That life is worth living is the most necessary of assumptions, and, were it not assumed, the most impossible of conclusions," in *The Life of Reason*, 1905.

Make an Offer

• A Westchester County, N.Y., internist sent us an ad which reads: "DAUGHTERS GONE – HORSES STAYED – 2 registered Appaloosa geldings, saddles, tack. Reasonable—make offer." It's practically a movie script. . . .